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XANTHOMATOSIS

CORRELATION OF CLINICAL, HISTOPATHOLOGIC AND CHEMICAL STUDIES OF CUTANEOUS XANTHOMA

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The concepts of cutaneous xanthomas of various types have been broadened and greatly changed in the last two decades. Many separate and interrelated factors, such as the relative amounts of the various lipoids in the blood,[1] the role played by the liver [2] and the pituitary gland,[3] by vitamins A and D and by diets [4] and descriptions of some

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1. (*a*) Bloch, Bruno: Metabolism, Endocrine Glands and Skin-Diseases, with Special Reference to Acne Vulgaris and Xanthoma, Brit. J. Dermat. **43**:61-87 (Feb.) 1931. (*b*) Schaaf, F., and Werner, A. J.: Die Pathogenese der Xanthome. Die Beziehungen von Cholesterin-, Phosphatid- und Gesamtfettgehalt des Blutes zur Entstehung der Xanthome, Arch. f. Dermat. u. Syph. **162**:217-239, 1930.

2. (*a*) Chaikoff, I. L.; McGavack, T. H., and Kaplan, A.: The Blood Lipids in the Postabsorptive State and After the Ingestion of Fat in Normal Human Subjects and in a Case of Disseminated Cutaneous Xanthomata, J. Clin. Investigation **13**:1-13 (Jan.) 1934. (*b*) Kyrle, Joseph: Histobiologie der menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925, vol. 1, pp. 291-301. (*c*) McGavack, T. H., and Shepardson, H. C.: Xanthoma Accompanied by Hypercholesterolemia, Occurring in an Otherwise Normal Individual, and in an Individual with Acromegaly and Diabetes, Ann. Int. Med. **7**:582-604 (Nov.) 1933. (*d*) Schilling, Wilhelm: Xanthelasma und Ikterus. Xanthomatose mit Leberzirrhose, Deutsche med. Wchnschr. **60**:972-975 (June 29) 1934.

3. (*a*) Rowland, R. S.: Xanthomatosis and the Reticulo-Endothelial System: Correlation of an Unidentified Group of Cases Described as Defects in Membranous Bones, Exophthalmos and Diabetes Insipidus (Christian's Syndrome), Arch. Int. Med. **42**:611-674 (Nov.) 1928. (*b*) Weidman, F. D.: Position of "Pseudodiabetic Xanthoma" Among the Lipoid Disturbances of the Skin (Urbach), Arch. Dermat. & Syph. **35**:815-820 (May) 1937. (*c*) Weidman, F. D., and Schaffer, H. W.: Xanthoma of the Skin and Larynx Associated with Carcinoma of the Stomach and a Regressive Xanthoma of the Pons, ibid. **35**:767-814 (May) 1937. (*d*) McGavack and Shepardson.[2c]

(Footnotes continued on next page)

unusual forms of xanthoma, like lipoid proteinosis (lipoidosis cutis et mucosae [5]), in which there apparently is primarily a disturbance of the phosphatide metabolism, have made the problem more complex. Cases of the Hand-Schüller-Christian syndrome and of Niemann-Pick's disease in which there were cutaneous xanthomatous lesions have been reported.[6] Hepatosplenomegaly [7] (lipoidosis of the skin and the mucous membranes), as described by Bürger and Grutz, and Gaucher's disease belong in the category of systemic xanthomatoses.[8]

Space does not permit us to discuss the various classifications of xanthomas recently [9] given, except to concur with Polano [10] in distinguishing between xanthoma tuberosum and disseminate xanthomatosis (xanthelasma disseminatum). We shall attempt to correlate the results of clinical, histopathologic and chemical studies in cases of xanthoma observed at the Mayo Clinic. Emphasis will be placed on variations in the lipoid contents of blood and tissue and on systemic manifestations of xanthoma, especially in regard to cardiovascular disease. References to the older literature regarding xanthoma were given in a previous paper [11] and are thoroughly discussed by Urbach.[5]

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4. (*a*) Schönheimer, Rudolf: Ueber eine Störung der Cholesterin-Ausscheidung (Ein Beitrag zur Kenntnis der Hypercholesterinämien), Ztschr. f. klin. Med. **123**: 749-763, 1933. (*b*) Thannhauser, S. J.: Cholesterol from Its Chemical, Physiological, and Clinical Aspects, to be published. (*c*) Wiedmann, Albert: Untersuchungen zur Frage der Ätiologie des Xanthoma tuberosum, Arch. f. Dermat. u. Syph. **175**:71-77 (Jan.) 1937.

5. Urbach, Erich: Lipoidstoffwechselerkrankungen der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 2, pp. 238-374.

6. (*a*) Chester, William, and Kugel, V. H.: Lipoidgranulomatosis (Type, Hand-Schüller-Christian): Report of a Case, Arch. Path. **14**:595-612 (Nov.) 1932. (*b*) McGraw, A. B.: Juvenile Xanthoma Multiplex: Case Report and Discussion of the Literature, Am. J. Cancer **18**:345-356 (June) 1933. (*c*) Wood, V. V.: Bilateral Xanthomatosis Lipoidosis of Mastoids: Case Report, to be published.

7. Bürger, M.: Das Cholesterinproblem in der inneren Medizin, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **43**:186-207, 1931. Urbach.[5]

8. Pick, Ludwig: (*a*) A Classification of the Diseases of Lipoid Metabolism and Gaucher's Disease, Am. J. M. Sc. **185**:453-469 (April) 1933; (*b*) Niemann-Pick's Disease and Other Forms of So-Called Xanthomatosis, ibid. **185**:601-616 (May) 1933.

9. (*a*) Melicow, M. M.: Xanthic Lesions: Report of Four Cases, Including Two of "Xanthomatosis" of the Kidney, J. A. M. A. **105**:768-774 (Sept. 7) 1935. (*b*) Siemens, H. W.: Zur Kenntnis der Xanthome, Arch. f. Dermat. u. Syph. **136**:159-197, 1921. (*c*) Urbach.[5]

10. Polano, M. K.: Ueber die Pathogenese der Cholesterosen der Haut, Arch. f. Dermat. u. Syph. **174**:213-224, 1936.

11. Finney, W. P.; Montgomery, Hamilton, and New, G. B.: Xanthoma Multiplex: Two Cases Involving the Larynx and Trachea, and Associated with Diabetes Insipidus, J. A. M. A. **99**:1071-1074 (Sept. 24) 1932.

MATERIAL FOR STUDY

This study is based on fifty cases of various types of cutaneous xanthoma, in thirty-five of which the diagnosis was proved histologically. Chemical studies of the blood were made in thirty-seven cases and in eleven of these cases quantitative chemical studies of the different lipoids contained in the cutaneous nodules were made at the same time. In some of these thirty-seven cases the chemical studies were only partially complete or were done by older methods of analysis,[12] so that only an increase or a decrease in one or more of the lipoids was indicated, without any means of accurate comparison being afforded. In none of the fifty cases was there any clinical or laboratory evidence of the Hand-Schüller-Christian syndrome or of Niemann-Pick's or Gaucher's disease.

In addition, thirty-eight cases of xanthoma of the eyelids (xanthelasma) were reviewed, seventeen of them by histologic examination and nine by chemical analysis of the blood. Thirteen cases of so-called xanthic tumors of the tendon sheaths were studied histologically, and in three cases of dermatofibroma (histiocytoma) [13] chemical studies of both the blood and the tissues and histologic examinations were made.

Histologic observations for the entire series of cases were based on studies of frozen sections stained with scarlet red, sudan III and frequently nile blue. Other stains for various lipoids were not employed, as we believe that chemical studies of tissue are more reliable than histologic examination. The same is true regarding polariscopic observations for doubly refractile lipoids. Histologic studies were made of sections of tissue fixed with alcohol and with solution of formaldehyde and stained with routine preparations, including hematoxylin and eosin, Van Gieson's stain, various stains for elastic tissue, the Maersch-Bielschowsky stain for *Gitterfäsern* and at times stains for hemosiderin, melanin, mucin and amyloid.

Determinations of carotene were made in several instances. Most of the patients were of normal or even subnormal weight. In cases in which there was an increase in the various lipoids in the blood in association with obesity the lipemia exceeded by far any increase in circulatory lipoids attributable to this factor. No determinations were made of the iodine number of the blood.[14]

CHEMICAL STUDIES OF THE BLOOD AND THE TISSUE

Because of variations in the normal figures for the various blood lipoids by different methods of analysis and because of the lack of uniformity in estimations of the lipoid content of normal skin, the

12. Weidman, F. D., and Sunderman, F. W.: Hypercholesterolemia: I. The Normal Blood Cholesterol Figures for Man and for the Lower Animals, Arch. Dermat. & Syph. **12**:679-690 (Nov.) 1925.

13. Senear, F. E., and Caro, M. R.: Histiocytoma Cutis, Arch. Dermat. & Syph. **33**:209-225 (Feb.) 1936.

14. Epstein, N. N., and Glick, David: Unsaturated Fatty Acids in Eczema: Observations on Acne Vulgaris, Psoriasis, Xanthoma Tuberosum, and Xanthoma Palpebrarum, Arch. Dermat. & Syph. **35**:427-432 (March) 1937.

following brief résumé of the method employed is given. The normal values for lipoids in the blood employed at the clinic are given in table 1.

The phosphatide phosphorus content may be obtained by dividing the figure for lecithin by 25. The determination of lecithin is separate from that of total lipoids. In our calculations the total cholesterol plus the total fatty acids (which includes the neutral fats and lecithin) equals the total lipoids.

Tabulation of the percentage of total cholesterol and of lecithin in the total lipoids readily reveals any increase or decrease in either cholesterol or lecithin. Probably because of articles in the literature dealing with the antagonistic action of cholesterol and lecithin (phosphatide phosphorus × 25) in the forming of cholesterol and lipoid emulsions, Schaaf [15] gave a formula for the relationship of the combined cholesterol to the phosphatide phosphorus. This can be worked out readily in our tables in those cases in which both lecithin and cholesterol esters (combined cholesterol) were studied; however, the expression of some of our figures in this ratio only seemed to accentuate differences in figures which were readily understood when expressed in terms of percentage of the total lipoids.

The figures for blood lipoids given in the tables should be compared with the normal values (table 1). The figures for the chemical constituents of tissue are given in percentages of the wet weight of the specimen. In all cases the sub-

TABLE 1.—*Normal Values for Lipoids in the Blood*

	Mg. per 100 Cc. Plasma	Average	Percentage of Total Lipoids
Total cholesterol	160-200	180	34
Cholesterol esters	110-145	125	70*
Lecithin	200-250	225	43†
Total fatty acids	335-350	345	66
Total lipoids	500-550	525	100

* Percentage of total cholesterol.
† Calculated as percentage of total lipoids but included in fatty acids.

cutaneous fat and the adjacent normal tissue were carefully trimmed from the xanthomatous nodule. In determinations on normal skin or skin adjacent to xanthoma the subcutaneous fat was cut off. The figures for the chemical constituents of tissue in the tables are given in percentages of the total lipoids, for purposes of comparison with the percentages of lipoids in the blood. The weight of the specimens of tissue in cases in which accurate analysis was possible varied from 150 to 1,000 mg., wet weight. Immediate analysis was made.

The figures for lipoids in blood and tissue, we believe, are accurate within the percentage of error of the methods used. In several cases studies of lipoid in the blood made a day apart revealed almost identical figures. The normal variation in the various lipoids in the blood (table 1) is based on a correlation of studies made in cases of many other conditions. Studies on lipoids in the blood were all made in the morning, without the patient's having had breakfast, and most of the specimens for study of tissue were taken at this time.

The methods of analysis for both blood and tissue were as follows:

In the determination of the amounts of various lipoids in the blood the procedures were carried out on plasma. Cholesterol was determined by the method

15. Schaaf, Fritz: Experimentelle Beiträge zur Pathogenese der Xanthome, Arch. f. Dermat. u. Syph. **175**:279-333 (Feb.) 1937.

of Bloor,[16] lecithin by the Whitehorn procedure[17] and total lipoids by the technic outlined by Bloor.[18] The determinations of these same substances in tissue were carried out by the same procedures on the alcohol-ether extract of the tissues. With fragile and easily disintegrated tissues the lipoids were extracted by grinding with sand several times in the presence of alcohol and ether. Extractions were considered complete when the last extract contained no lipoids. For the more fibrous types of tissue we resorted to preliminary hydrolysis with alcohol and potassium hydroxide, as mentioned by Wile and his associates,[19] followed by extraction of the acidified hydrolysate with alcohol and ether. Comparative results for tissues extracted by grinding with sand in the presence of alcohol and ether and by preliminary hydrolysis with alcoholic potassium hydroxide followed by alcohol-ether extraction were in good agreement.

The normal figures for the lipoids in the skin vary considerably. Wile, Eckstein and Curtis[20] have shown that 20 per cent of the lipoids in the epidermis and only 0.25 per cent of those in the subcutaneous tissues are in the form of cholesterol. They found only 2.8 per cent of cholesterol in sebum, 1.43 per cent in sweat from the hands and 19.6 per cent in the horny layer of skin.[21] Engman and Kooyman[22] found somewhat higher figures. Bloch[1a] has emphasized, however, that one should compare the lipoid content of the xanthomatous nodules not with that of the epidermis but with that of the skin as a whole.

Usher and Rabinowitch[23] in a recent review of the literature found that the total lipoids vary between 0.97 and 4.4 per cent in normal skin but are as high as 7 or 8 per cent in skin from patients with exfoliative dermatitis. Wile, Cameron and Eckstein[19] in a recent study gave 1.11 to 2.9 per cent as the total lipoid content of normal skin. Usher in one case found the total lipoids to be 3.26 per cent for normal skin, 15 per cent of this being in the form of cholesterol. Usher[24] in an analysis of a series of specimens of normal skin found the total lipoids to vary from 1.3 to 2 per cent, the cholesterol amounting to from 7.5 to

16. (*a*) Bloor, W. R.: The Determination of Cholesterol in Blood, J. Biol. Chem. **24**:226-231, 1916. (*b*) Bloor, W. R., and Knudson, Arthur: The Separate Determination of Cholesterol and Cholesterol Esters in Small Amounts of Blood, ibid. **27**:107-112, 1916.

17. Whitehorn, J. C.: A Method for the Determination of Lipoid Phosphorus in Blood and Plasma, J. Biol. Chem. **62**:133-138 (Nov.) 1924.

18. Bloor, W. R.: The Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77**:53-73 (April) 1928.

19. Wile, U. J.; Cameron, O. J., and Eckstein, H. C.: Effect of the Roentgen Rays on the Lipids of the Epidermis, Arch. Dermat. & Syph. **32**:69-72 (July) 1935.

20. (*a*) Eckstein, H. C., and Wile, U. J.: Lipid Studies in Xanthoma, J. Biol. Chem. **87**:311-317 (June) 1930. (*b*) Wile, U. J.; Eckstein, H. C., and Curtis, A. C.: Lipid Studies in Xanthoma, Arch. Dermat. & Syph. **19**:35-51 (Jan.) 1929; (*c*) Lipid Studies in Xanthoma: Further Contribution, ibid. **20**:489-500 (Oct.) 1929.

21. Eckstein, H. C., and Wile, U. J.: The Cholesterol and Phospholipid Content of the Cutaneous Epithelium of Man, J. Biol. Chem. **69**:181-186 (July) 1926.

22. Engman, M. F., and Kooyman, D. J.: Lipids of the Skin Surface, Arch. Dermat. & Syph. **29**:12-19 (Jan.) 1934.

23. Usher, B., and Rabinowitch, I. M.: Necrobiosis Lipoidica Diabeticorum: Report of a Case with Clinical, Pathologic and Biochemical Observations, Arch. Dermat. & Syph. **35**:180-187 (Jan.) 1937.

24. Usher, B.: Personal communication to the authors.

16 per cent and the lecithin to from 10 to 30 per cent of the total lipoids. Both he and Wile found the largest part of the cholesterol in free form. In our studies the skin adjacent to a xanthomatous tumor nodule in two instances revealed only traces of cholesterol and cholesterol esters and gave a total lipoid content of 3.9 per cent. Three other determinations on normal skin gave total lipoid contents varying from 0.9 to 2.07 per cent. Again, the cholesterol and cholesterol esters varied from mere traces to 15 per cent of the total lipoids. Lecithin varied from only traces up to 27 per cent of the total lipoids.

We may assume, therefore, that the amount of total lipoids of normal skin averages less than 3 per cent of the wet weight, that from 5 to 15 per cent of these total lipoids is in the form of cholesterol (most of it being free) and that the lecithin varies from only a trace up to 30 per cent of the total lipoids. A larger series of analyses of the normal lipoid content of skin of different thicknesses from various parts of the body is needed.

NEVOXANTHO-ENDOTHELIOMA

There were two cases of nevoxantho-endothelioma in our series of fifty cases of various types of xanthoma.

The first case was reported briefly elsewhere [25] (fig. 1). Two analyses of the chemical constituents of the blood revealed the amount of cholesterol, of fatty acids and of total lipoids to be within normal limits, although the amounts of cholesterol in the total lipoids were 39 and 54 per cent in the two determinations. In the second case the total cholesterol was 119, the fatty acids 212 and the total lipoids 331 mg. per hundred cubic centimeters of plasma, all factors being subnormal. The cutaneous lesions developed in these two cases when the patients were aged 5 and 7 months, respectively, and in the second case all but one had undergone involution two years later. In neither case was there any family history of similar lesions. In both cases there was a typical histologic picture, characterized not only by foam cells containing various lipoids and by Touton giant cells, but by definite proliferation of the endothelium of the capillaries and smaller blood vessels in the upper part of the cutis, resulting in the formation of endothelial giant cells (fig. 1).

The presence of many endothelial giant cells and the proliferation of endothelial cells and connective tissue histiocytes, with relatively few xanthoma cells, distinguishes this condition histologically from juvenile xanthoma. Furthermore, the clinical spontaneous involution of these lesions over a period of years, together with the fact that the lipoid content of the blood fell within normal limits in the two cases we have studied, justifies separating the disease from juvenile xanthoma. Senear and Caro [26] found a normal value for blood cholesterol in their case; they, however, allied their case to those of juvenile xanthoma.

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25. Montgomery, Hamilton: Nevoxanthoendothelioma, in Nekam, L.: Corpus Iconum Morborum (Iconographia), Budapest, to be published.

26. Senear, F. E., and Caro, M. R.: Nevoxantho-Endothelioma or Juvenile Xanthoma, Arch. Dermat. & Syph. **34**:195-206 (Aug.) 1936.

Two other cases of nevoxantho-endothelioma have recently been reported.[27] The presence of foam cells and occasional Touton giant cells in the histologic sections definitely stamp this condition, we believe, as a variant of cutaneous xanthoma. McDonagh's designation of the condition in this group of cases as nevoxantho-endothelioma has resulted in some confusion, because there is simply a proliferation of endothelial cells to form endothelial giant cells and no true tumor formation, such as that which occurs in so-called endothelioma of the skin, particularly hemangio-endothelioma.

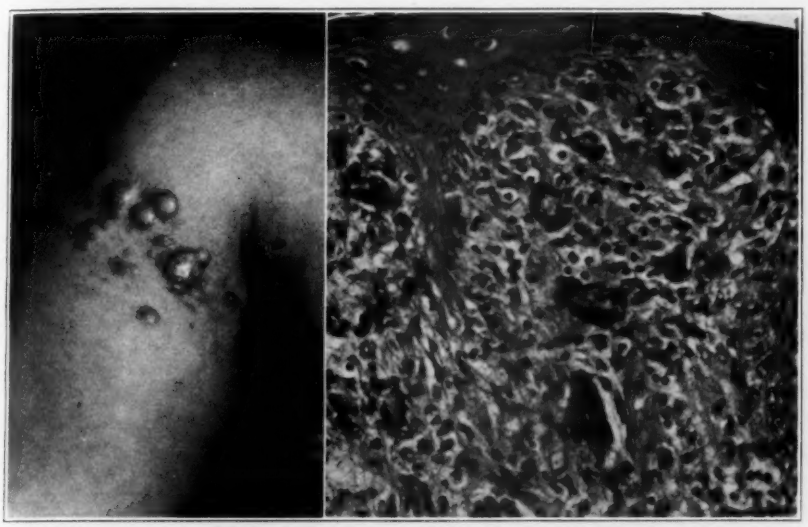

Fig. 1.—Nevoxantho-endothelioma, showing typical grouped lesions. Endothelial and Touton type giant cells and the proliferation of capillary endothelium can be seen. Relatively few foam cells are present.

JUVENILE XANTHOMA

Two of the fifty cases of xanthoma fell into the group of juvenile xanthoma:

The first was that of a boy aged 4 years, who had had lesions since the age of 6 months. Multiple xanthomas of the flat type were distributed over the neck, the arms, the lower part of the back, the gluteal region and the legs. They formed plaques, especially on the extensor surfaces, as contrasted with the discrete lesions of nevoxantho-endothelioma. The family history was irrelevant, as were the results of general examination. The histopathologic picture was indistinguishable from that of ordinary cutaneous xanthoma and showed a predominance of foam

27. (*a*) Adamson, H. G.: A Note on Multiple Eruptive Xanthoma in Infants: Naevoxantho-Endothelioma (McDonagh), Brit. J. Dermat. **48**:366-370 (July) 1936. (*b*) Lamb, J. H., and Lain, E. S.: Nevo-Xantho-Endothelioma: Its Relationship to Juvenile Xanthoma, South. M. J. **30**:585-594 (June) 1937.

cells, including Touton giant cells; there were no endothelial giant cells. Studies of the blood revealed a normal value for cholesterol (172 mg. per hundred cubic centimeters, or 15 per cent of the total lipoids), but a marked increase in fatty acids (883 mg.) and in total lipoids (1,044 mg.). The sugar content of the blood was normal, as was the patient's weight. After administration of a diet in which the caloric intake was limited, the lesions gradually underwent involution. Six years later Dr. W. H. Alexander, of Iron Mountain, Mich., reported that the patient had stayed on the diet and had remained free from lesions for two years.

The second patient, a girl aged 19 years, had had an attack of jaundice at the age of 10 years, followed by yellowish papules at the sites of trauma. She presented the picture of xanthoma tuberosum and had multiple xanthomas on the extensor surfaces and the tendon sheaths. The sugar content of the blood and the hepatic function were normal. Roentgenograms showed no abnormality. There were 641 mg. of cholesterol, 653 mg. of fatty acids, 1,294 mg. of total lipoids per hundred cubic centimeters of plasma, the cholesterol representing 50 per cent of the total lipoids. The patient was underweight.

Weidman and Freeman [28] described the case of a boy, aged 9 years, who had had cutaneous lesions of both xanthoma tuberosum and disseminate xanthomatosis of eleven months' duration. He had had jaundice several years previously and again following an injury to the skull eighteen months previously. Symptoms of diabetes insipidus developed three months before the patient was seen. The cholesterol content of the blood was elevated. Postmortem examination revealed an enlarged liver and xanthomas involving the liver, the skull, the brain and the pituitary body. This case was subsequently classified by Chester and Kugel as one of Hand-Schüller-Christian disease.

Both of our cases, especially the second, might be classified as instances of xanthoma tuberosum. Less frequent than that disease are the disseminate forms of xanthomatosis, and rarely is there a combination of both with Hand-Schüller-Christian disease. Juvenile xanthoma is characterized frequently by the history of familial occurrence,[29] often by an increase in cholesterol and in total lipoids [30] and frequently by the occurrence of severe cardiac disease.[31] Usually the mitral valve and the myocardium are involved, but at times the coronary arteries have

28. Weidman, F. D., and Freeman, Walter: Xanthoma Tuberosum: Two Necropsies Disclosing Lesions of the Central Nervous System and Other Tissues, Arch. Dermat. & Syph. **9**:149-175 (Feb.) 1924.

29. (*a*) Beeson, B. B., and Albrecht, P. G.: A Contribution to the Study of Xanthoma Tuberosum, with Report of a Case, Arch. Dermat. & Syph. **8**: 695-710 (Nov.) 1923. (*b*) Lane, C. G., and Goodman, Joseph, Jr.: Xanthoma Tuberosum: Report of Familial Occurrence with Probable Cardiac Lesions, ibid. **32**:377-384 (Sept.) 1935. (*c*) Levin, E. A., and Sullivan, Maurice: Familial Xanthoma: Report on Three of Five Siblings with Xanthoma Tuberosum Multiplex, ibid. **33**:967-969 (June) 1936. (*d*) Wile, U. J., and Duemling, W. W.: Familial Xanthoma, ibid. **21**:642-647 (April) 1930.

30. (*a*) Brandt, H.: Ein Fall von generalisierter Xanthomatose mit Dysregulation innerhalb des Lipoidstoffwechsels, Dermat. Wchnschr. **100**:11-17 (Jan. 5) 1935. (*b*) Levin and Sullivan.[29c] (*c*) Beeson and Albrecht.[29a]

31. Lane and Goodman.[29b] McGraw.[6b] Wile and Duemling.[29d]

been involved, a point which has been confirmed by postmortem examinations.[32] A familial history of both xanthoma and cardiac disease is not infrequent.

XANTHOMA TUBEROSUM

The following case is typical of the twenty-six cases of xanthoma tuberosum in adults:

A married woman aged 47 was seen at the clinic in August 1933 because of obesity and the presence of yellowish nodules in the skin of six years' duration. She was 5 feet 6 inches (168 cm.) tall and weighed 195 pounds (88.5 Kg.). Examination revealed typical nodules of xanthoma tuberosum on her elbows, her heels and

Fig. 2.—Xanthoma tuberosum, showing typical lesions on the extensor surfaces.

the extensor tendons of the hand (fig. 2), typical lesions of xanthoma palpebrarum and some smaller xanthomatous papules over the shoulders and the buttocks. The family history was irrelevant. Results of studies of the blood and the tissue are given in table 2. The sugar and urea contents of the blood were within normal limits, and a test of hepatic function showed no abnormality. A roentgenogram of the skull showed a calcified pineal gland. Histologic studies of various nodules removed at different times for chemical study revealed the typical picture of xanthoma.[33]

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32. Hess, F. O.: Ueber allgemeine Xanthomatose, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **46**:355-359, 1934. McGraw.[6b]

33. Gans, Oskar: Histologie der Hautkrankheiten die Gewebsveränderungen in der kranken Haut unter Berücksichtigung ihrer Entstehung und ihres Ablaufs, Berlin, Julius Springer, 1925, vol. 1, pp. 136-147. Kyrle.[2b]

In 1933, under a dietary regimen which had consisted of 550 calories and 250 Gm. of additional carbohydrate, the patient had experienced a marked drop in blood lipoids and had lost 30 pounds (15.6 Kg.). Appreciable involution of the cutaneous lesions had occurred at that time. Examination in May 1935 showed no new lesions. There were no lesions in the larynx or the pharynx. New lesions developed during the winter of 1936. When the patient was examined in September 1936, she weighed 192 pounds (87.1 Kg.) and had definite symptoms of intermittent claudication after walking a few blocks. There was pain in her chest, which cardiovascular examination revealed to be coronary sclerosis accompanied with mild angina. On a diet low in cholesterol and free from animal fats, as advocated by Schönheimer,[4a] she again lost 30 pounds (15.6 Kg.), and there was improvement in the condition of the blood. The patient was seen again in January 1937, at

TABLE 2.—*Studies of Blood and Tissue in the First Case of Xanthoma Tuberosum*

			After Diet				After Diet	
	Amount*	Percentage of Total Lipoids	Amount*	Percentage of Total Lipoids	Amount*	Percentage of Total Lipoids	Amount*	Percentage of Total Lipoids
Date	8/12/33		9/1/33		10/2/36		1/7/37	
Blood								
Total cholesterol	672	27	206	29	617	36	362	38
Cholesterol esters	...	..	...	..	555	90†	298†	82†
Lecithin	492	20‡	286	40‡	454	27‡	478	50‡
Fatty acids	1,825	73	506	71	1,078	64	593	62
Total lipoids	2,497	..	712	..	1,695	..	955	..
Date	8/12/33		9/1/33		9/30/36§		9/30/36¶	
Tissue								
Total cholesterol	4.34	53	6.37	51	2.7	49	2.4	44
Cholesterol esters	2.64	61†	4.28	67†	2.0	74	1.5	62†
Lecithin	1.8	22‡	2.21	18‡	1.4	25‡	2.1	37‡
Fatty acids	3.79	47	6.18	49	2.8	51	3.05	56
Total lipoids	8.13	..	12.55	..	5.5	..	5.45	..

* Values for the blood are expressed in milligrams per hundred cubic centimeters of plasma; those for the tissue, in percentage of the wet weight.
† Expressed as percentage of cholesterol.
‡ Calculated as percentage of total lipoids but included in fatty acids.
§ Old tumor nodule.
¶ New tumor nodule.

which time the anginal pains were more marked, as were the symptoms of intermittent claudication. Considerable involution of several of the remaining xanthomas had occurred at that time.

An analysis of other cases of xanthoma tuberosum is given in table 3. (Case 3 was that of a solitary posttraumatic lesion.) In all cases the lesions occurred predominantly on the extensor surfaces (fig. 2). There were no lesions of the mucous membranes. In case 6 there was a family history of diabetes, and the patient showed definite signs of intermittent claudication and was therefore put on a diet low in cholesterol and free from animal fat. There was improvement in the amount of lipoids in the blood, but symptoms suggestive of avitaminosis (vitamin A) have developed. In none of these cases was there a family history of xanthoma. The cholesterol content of the xanthomatous nodules in all cases was above normal, reaching as high as 64

per cent of the total lipoids and dropping to 18 per cent only in an old fibrous nodule which histologically revealed few foam cells. This cholesterol content of the total lipoids was greatly above that found in normal epidermis, and in six of seven cases it exceeded the normal ratio for lipoids in the blood. From 60 to 90 per cent of the cholesterol was in combined form. The increase in lecithin in case 7 may be explained in part by the demonstration in frozen section of the extracellular deposit of much of the lipoids. Chemical analysis in

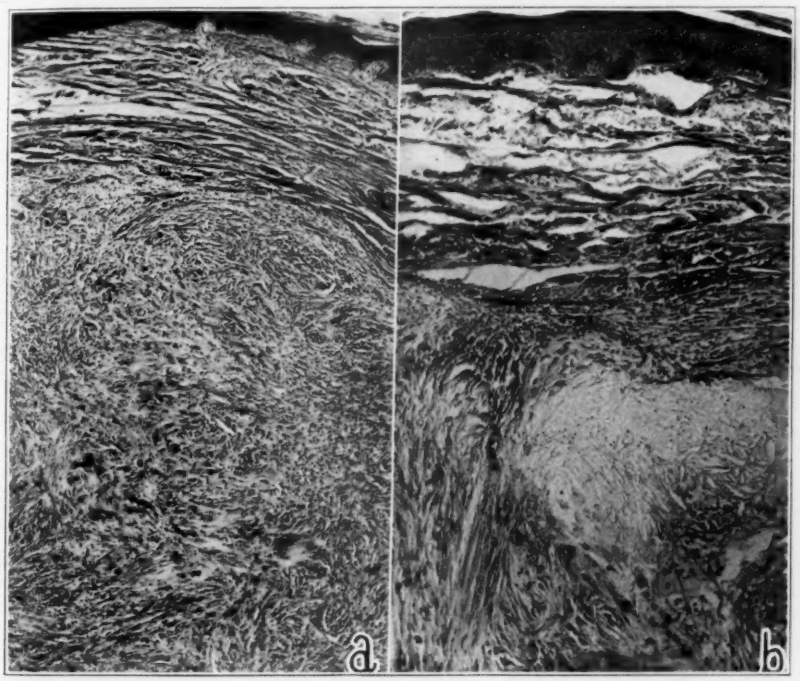

Fig. 3.—Xanthoma tuberosum, showing *a*, fibrous stage of involution resembling the picture seen in dermatofibroma (histiocytoma); *b*, xanthoma tuberosum and fibrosis, with a large area showing the deposit of cholesterol crystals and an area of xanthoma cells immediately below that.

another case was made of a lesion involving the achilles tendon, but the weight of the wet tissue was only 50 mg., cholesterol being found to comprise 1.2 per cent of the weight of the tissue. No lecithin or uric acid was present. It is to be emphasized that changes in the various lipoids in blood and tissue are not parallel.

Studies of lipoids in the blood were made in ten cases of xanthoma tuberosum in addition to those given in table 3. All these cases showed an increase in total cholesterol (416 to 617 mg.) and in total lipoids

TABLE 3.—*Xanthoma Tuberosum*

Case	Age, Years	Sex	Date	Duration, Years	Other Findings	Biochemical Studies	Blood		Tissue		Histologic Observations
							Mg. per 100 Cc. of Plasma	Percentage of Total Lipoids	Percentage of Tissue	Percentage of Total Lipoids	
2	36	M	1/ 7/29	14	Exophthalmic goiter	Total cholesterol	...	..	1.63	18	Old fibrous lesion, few foam cells
						Cholesterol esters	...	..	1.35	83*	
						Fatty acids	...	..	7.45	82	
						Total lipoids	...	..	9.08	..	
3	45	M	7/26/29	..	Solitary tumor of knee following trauma	Total cholesteral	235	44	4.5	54	Fibrosis but many foam cells
						Cholesterol esters	...	..	4.0	89*	
						Lecithin †	312	58†	....	..	
						Fatty acids	300	56	3.77	46	
						Total lipoids	535	..	8.2	..	
4‡	40	F	7/11/29	..	None	Total cholesterol	313	41	8.9	64	Typical xanthoma
						Fatty acids	452	59	5.1	36	
						Total lipoids	765	..	14.0	..	
5‡	33	F	1/ 5/35	1	Common duct stricture, cirrhosis, obstructive jaundice	Total cholesterol	303	39	2.84	42	Typical xanthoma
						Cholesterol esters	...	..	2.3	81*	
						Lecithin †	446	57†	2.9	43†	
						Fatty acids	483	61	3.93	58	
						Total lipoids	786	..	6.77	..	
6	49	F	4/14/36	..	Occlusive arterial disease, intermittent claudication	Total cholesterol	657	39	4.6	51	Fibrosis but many cholesterol crystals
						Cholesterol esters	...	..	2.8	61*	
						Lecithin †	...	..	2.0	22†	
						Fatty acids	1,050	61	4.4	49	
						Total lipoids	1,675	..	9.0	..	
7‡	47	M	4/20/37	10	Cholecystitis, obesity (grade 3), early coronary sclerosis	Total cholesterol	256	32	1.42	38	Fibrosis, some foam cells
						Cholesterol esters	194	76*	0.81	57*	
						Lecithin †	328	41†	3.3	89†	
						Fatty acids	547	68	2.3	62	
						Total lipoids	803	..	3.7	..	

* Expressed as percentage of cholesterol.
† Calculated as percentage of total lipoids but included in fatty acids.
‡ Also xanthoma palpebrarum.

(941 to 1,633 mg.) per hundred cubic centimeters of plasma. As a rule, the cholesterol was elevated at the expense of the fatty acids and exceeded the normal ratio (percentage of total cholesterol to total lipoids). When the hyperlipemia was marked, however, the total cholesterol did not show as great an increase and therefore was in a lower proportion to the total lipoids. Reduction in the hyperlipemia and diminution in the size and number of the lesions on a low caloric diet occurred in several cases.

Analysis of the systemic findings in this group of cases of xanthoma tuberosum and a discussion of the lipoid chemistry will be given later. Cases showing similar changes in the lipoid content of blood [34] and tissue have been reported in the literature.[35]

EXTRACELLULAR CHOLESTEROSIS

Two cases in this series of fifty might well have been considered examples of extracellular cholesterosis.[36]

A girl aged 13 years was seen at the clinic in January 1928 because of cutaneous lesions on the extensor surfaces of four years' duration. These had developed after an injury to her foot and a diagnosis of xanthoma tuberosum multiplex was made. The family history and general examination showed nothing relevant. Studies of the blood revealed the urea, the uric acid, the sugar and the chloride content to be within normal limits. Doubly refractile bodies were present in the urine. Trauma to the dorsum of the hand resulted in the development of a new lesion. Specimens for biopsy from an old lesion and from this traumatically produced lesion showed that cholesterol and cholesterol esters were deposited intracutaneously in foam cells and fixed connective tissue cells about the blood vessels and extracellularly. There were marked deposits of hemosiderin about the blood vessels. In many areas numerous foam or xanthoma cells were evident in sections of material fixed with solution of formaldehyde and alcohol (fig. 4*a*). The diagnosis of a fibrous stage of xanthoma tuberosum, made by one of us (Montgomery), was questioned at the Dermatological Conference of the Mississippi Valley in October 1929, and at the meeting of the Minnesota Dermatological Society in February 1930, where the case was presented by Dr. Michelson [37] as possibly one of vegetative pyoderma. After Urbach's description of extracellular cholesterosis in 1932 this same case was reported by Laymon in 1937 [38] as

34. Irvine, H. G., and Turnacliff, D. D.: Xanthoma with Lipemia, Arch. Dermat. & Syph. **33**:898-899 (May) 1936.

35. Michael, J. C., and Nicholas, H. O.: Blood Lipids in Xanthoma, Arch. Dermat. & Syph. **29**:228-239 (Feb.) 1934. Polano.[19]

36. Urbach, E.; Epstein, E., and Lorenz, K.: Beiträge zur einer physiologischen und pathologischen Chemie der Haut: IX. Mitteilung. Extrazelluläre Cholesterinose, Arch. f. Dermat. u. Syph. **166**:243-272, 1932. Urbach.[5]

37. Michelson, H. E.: Chronic Vegetating Pyoderma, Arch. Dermat. & Syph. **22**:149 (July) 1030; Pyodermia Chronica Vegetans, ibid. **22**:533 (Sept.) 1930.

38. Laymon, C. W.: Extracellular Cholesterosis, Arch. Dermat. & Syph. **35**:269-284 (Feb.) 1937.

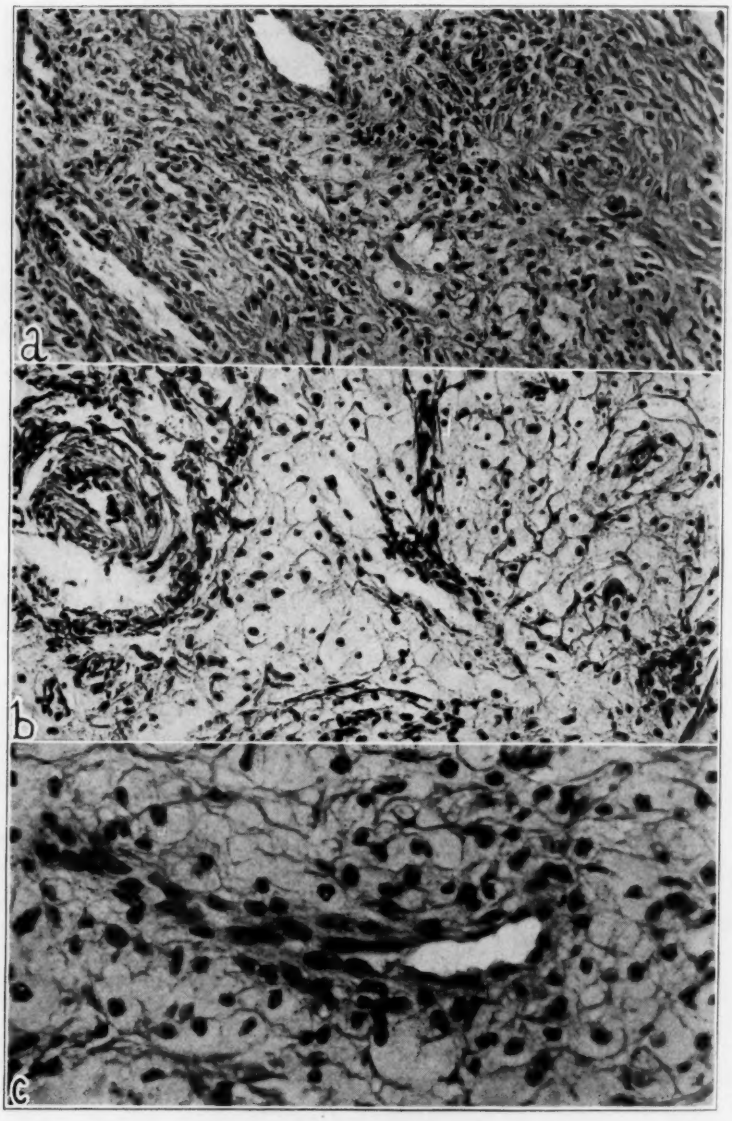

Fig. 4.—*a*, juvenile xanthoma, simulating extracellular cholesterosis with granulation tissue but with definite foam cells adjacent to small blood vessels; *b*, xanthoma tuberosum, showing typical foam cells involving the capillary walls and thickening and involvement of the wall of a large vessel; *c*, disseminate xanthomatosis, showing a picture similar to that of *b*. Even the endothelium of the blood vessel presents a foamy cytoplasm.

one of that disease, with a statement that the "history, photographs and sections were sent to Urbach, who studied them and concurred in the diagnosis of extracellular cholesterosis." Laymon obtained a normal value for blood cholesterol, and his clinical illustrations duplicated those taken at the clinic in January 1928. The histologic picture in a case presented by Dr. Duemling [39] before the Chicago Dermatological Society in May 1930 duplicated that seen in our case, and the clinical pictures in the two cases resembled each other closely. Duemling's case later proved to be one of xanthoma.[40]

The picture in both cases subsequently seemed to fit in clinically with that of extracellular cholesterosis. The presence of foam cells laden with lipoids would seem to rule out this diagnosis, and even Urbach's own illustrations in the "Handbuch" seem to indicate the presence of occasional foam and Touton giant cells. Urbach, on analyzing tissue in his case, found free cholesterol to be in a ratio of 3 to 1 to combined cholesterol, and there was hypolipemia in contrast to the reverse finding in cases of xanthoma tuberosum. This type of fibrous xanthoma with inflammatory and granulomatous changes deserves further study and investigation before one can justly put cases of this type in a separate group. Extracellular cholesterosis is to be differentiated from xanthelasma areolare multiplex of Riehl and Artz, which has yet to be proved a separate entity.

ATYPICAL MANIFESTATIONS

In a few cases accurate classification as to type of xanthoma was impossible:

One patient, a man aged 45, had pains in the joints and cutaneous lesions clinically resembling those of xanthoma tuberosum for ten years. There were no lesions of the mucous membranes. The amounts of the various lipoids in the blood were all within normal limits. The histopathologic picture showed not only marked fibrosis but areas of necrosis and questionable deposits of calcium in necrotic areas. The necrotic areas resembled the histologic picture seen in necrobiosis lipoidica diabeticorum. Lipoids in frozen section were deposited only in areas of necrosis or extracellularly. There was no history of diabetes.

A second patient, a man aged 34, had multiple lesions on the forehead, the cheeks and the ears, of two years' duration and clinically resembling adenoma sebaceum; they contained large amounts of cholesterol crystals and few xanthoma cells. Examination showed carotene. There was definite hyperlipemia, there being 347 mg. of cholesterol, 463 mg. of fatty acids and 810 mg. of total lipoids per hundred cubic centimeters of plasma. There was a definite reduction in the number of cholesterol cysts and in the amount of lipoids in the blood after the patient was given a reduction diet, the figures for the latter becoming 214 mg. of cholesterol, 446 mg. of lecithin, 377 mg. of fatty acids and 591 mg. of total lipoids per hundred cubic centimeters of plasma.

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39. Duemling, W. W.: A Case for Diagnosis, Arch. Dermat. & Syph. **23**:182 (Jan.) 1931.

40. Duemling, W. W.: Personal communication to the authors.

XANTHOMATOSIS DISSEMINATA

Table 4 gives the pertinent findings in cases of disseminate xanthomatosis. The first two cases were previously reported as instances of xanthoma multiplex,[11] but they are included here to give the results of analysis of tissue and the end-results. The third and the fourth case are of interest because of the diffuse yellowish red infiltration and coloration of the skin. The condition in case 3 resembled acne rosacea when superficial examination was made (fig. 5). Fine papular lesions were seen, especially on the flexural surfaces of the skin, and a few lesions were present on the extensors. A brief report of case 4 has been given by Chambers.[41] Xanthochromia, discrete, diffuse or even generalized, was seen in a minor degree in the first two cases and was seen occasionally in other cutaneous xanthomas or even independently of cutaneous lesions. The histopathologic changes corresponded to those seen in xanthoma tuberosum (figs. 4 and 6).

It is significant that in all these cases the amount of lipoids in the blood was essentially normal, in three cases being slightly below normal and only in one case (case 3) being elevated to a slight degree. The chemical constituents of the tumor, however, were similar to those in xanthoma tuberosum; there was a definite increase in the cholesterol content of the tumor as compared with that of the normal skin or with that of the blood. A lesion removed for chemical analysis in case 3 was too small to allow accurate quantitative determination. Cases similar to ours in which the blood has been essentially normal or its lipoid content only slightly elevated have been reported.[42] In none of these cases could involution of the cutaneous lesions be obtained under various dietary regimens. Weidman and Schaffer [3c] have just given a further report of Greenbaum's case [42a] under the title "pseudodiabetic xanthoma." In that case partial involution of the lesions occurred in association with the development of new ones.

In two other cases of xanthoma in this group the lesions were confined to the larynx and to the pharynx and the right anterior pillar of the tonsil, respectively.[43] Studies on the blood in one case showed low values for cholesterol and total lipoids. Difficulty in swallowing or breathing to a point necessitating operation is frequently encountered with disseminate xanthomatosis involving the mucous membranes. The incidence of diabetes insipidus in this group of cases warrants emphasis.

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41. Chambers, Stanley: Xanthomatosis, Arch. Dermat. & Syph. **34**:921 (Nov.) 1936.

42. (*a*) Greenbaum, S. S.: Xanthoma with Erythema Telangiectodes and Parapsoriasis, Arch. Dermat. & Syph. **13**:78-89 (Jan.) 1926. (*b*) Villela, G. G., and Rabello Jr.: Studies in Xanthoma: Biochemistry and Pathogenesis, Mem. Inst. Oswaldo Cruz **30**:305-325 (Dec.) 1935. (*c*) Polano.[10] (*d*) Siemens.[9b]

43. New, G. B.: Xanthoma of the Pharynx and Larynx, Arch. Otolaryng. **22**:449-453 (Oct.) 1935.

TABLE 4.—*Disseminate Xanthomatosis*

Case	Age, Yr.	Sex	Duration, Yr.	Parts Affected	Biochemical Studies	Before Low Fat Diet: Mg. per 100 Cc. of Plasma	Before Low Fat Diet: Percentage of Total Lipoids	After Low Fat Diet: Mg. per 100 Cc. of Plasma	After Low Fat Diet: Percentage of Total Lipoids	Tissue: Percentage of Tissue	Tissue: Percentage of Total Lipoids	Tissue: Percentage of Tissue	Tissue: Percentage of Total Lipoids	Histopathologic Observations	Results
1	27	M	4	Flexural surfaces, eyelids, trachea, pharynx, larynx, scrotum	Date	9/22/31		11/16/31		9/22/31		9/21/31		Typical xanthoma, many Touton giant cells	No response to low fat diet; died March 1933; xanthoma of trachea, larynx, bronchi, kidneys, hypophysis and tuber cinereum
					Total cholesterol	172	37	185	33	3.45	40	6.78	52		
					Cholesterol esters	...	..	166	90*	3.0	87*	6.1	90*		
					Lecithin	...	..	240	42†	2.58	30†	2.87	21†		
					Fatty acids	289	63	380	67	5.15	60	6.5	48		
					Total lipoids	461	..	565	..	8.60	..	13.50	..		
2	42	M	1½	Flexural surfaces, face, neck, eyelids, cornea, trachea, pharynx, larynx, anus, scrotum	Date	1/20/32		1/12/33		1/19/32				Typical xanthoma, many Touton giant cells	No response to low fat diet; myocardiac degeneration, large liver with dye retention of grade 2, ascites, cardiac decompensation; died 2/19/35
					Total cholesterol	167	38	116	31	4.55	56	....	..		
					Cholesterol esters	119	71*	73	63*	3.66	80*	....	..		
					Lecithin	246	56†	223	50†	2.23	27†	....	..		
					Fatty acids	273	62	260	69	3.64	44	....	..		
					Total lipoids	440	..	376	..	8.19	..	....	..		
3	48	F	½	Flexor and extensor surfaces, eyelids, mouth, tongue, face (diffuse erythema)	Date	6/26/36		3/6/37		.....		.....		Typical xanthoma, many Touton giant cells	Slight response to diet free of animal fat; progression of xanthoma in spite of control of diabetes with solution of posterior pituitary and aminopyrine
					Total cholesterol	214	41	231	36	....	..	....	..		
					Cholesterol esters	...	..	...	..	....	..	....	..		
					Lecithin	305	59†	297	46†	....	..	....	..		
					Fatty acids	302	59	405	64	....	..	....	..		
					Total lipoids	516	..	636	..	....	..	....			
4	42	M	2	Nasopharynx and septum, vocal cords, skin (diffuse yellowish discoloration)	Date	6/3/35		1/7/36		.....		.....		Typical xanthoma, Touton giant cells, sclerodermatous lesion	No response to low fat diet and linseed oil, February 1936
					Total cholesterol	124	31	151.5	..	....	..	....	..		
					Cholesterol esters	...	..	...	..	....	..	....	..		
					Lecithin	...	..	...	..	....	..	....	..		
					Fatty acids	270	69	...	..	....	..	....	..		
					Total lipoids	394	..	...	..	....	..	....	..		

* Expressed in percentage of cholesterol.
† Calculated as percentage of total lipoids but included in fatty acids.
Note: Patients in cases 1, 2 and 3 had diabetes insipidus; the patient in case 4 had questionable poikiloscleroderma.

XANTHOMA DIABETICORUM

Nine of the cases in this series were instances of xanthoma diabeticorum. In eight of these studies of the blood were made, but in only five by modern methods (table 5).

The cholesterol content of the blood which in some cases was not elevated in proportion to the amounts of other lipoids, did not drop as quickly on a therapeutic regimen as did the total fatty acids and total lipoids, so that the percentage of cholesterol approached normal or even became elevated above normal. One patient in this group, a woman aged 38 who had had diabetes for six years, died in the hospital of myocardiac degeneration, arteriosclerosis and hypertension. Postmortem

Fig. 5.—Disseminate xanthomatosis, showing diffuse rosacea-like erythema, scattered xanthoma including the eyelids and typical small papular xanthoma axillae comparable to xanthoma diabeticorum.

examination revealed hypertrophy of the heart, the liver and the kidneys, accompanied with fatty changes and atrophy of the pituitary gland.

The histologic picture of xanthoma diabeticorum may duplicate that of ordinary xanthoma, but biopsy performed as the lesions are undergoing involution because of a dietary regimen shows the cholesterol and other lipoids to lie extracellularly as well as intracellularly, especially about the blood vessels and in the connective tissue histiocytes. Few true foam cells are seen. The reticulo-endothelial system of the skin may be outlined by the deposits of lipoids.[44] There may be inflammatory

44. Pautrier, L. M.: Dermo-Epidermic Interchanges as Controlled by the Study of Melanin Pigment, the Esters of Cholesterol (Xanthoma) and Hemosiderin (Schamberg's Disease), Arch. Dermat. & Syph. **17**:1-13 (Jan.) 1928.

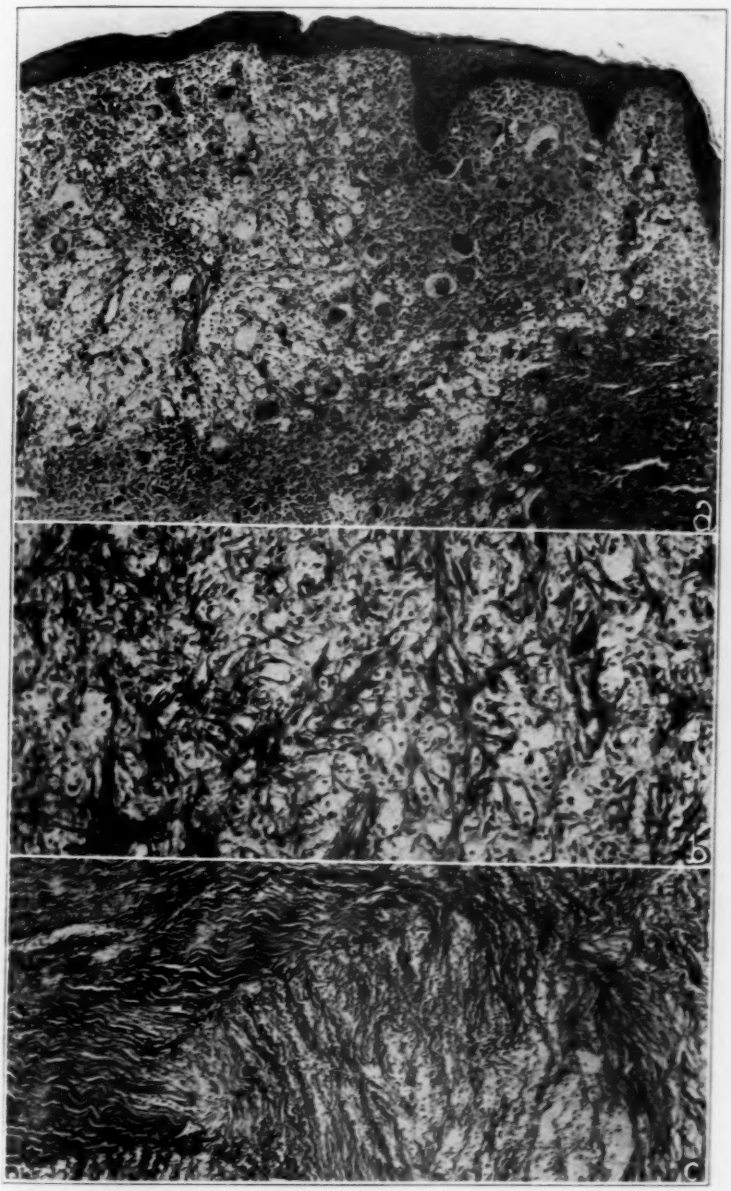

Fig. 6.—*a*, disseminate xanthomatosis, showing a typical picture, with foam cells about the blood vessels, numerous Touton giant cells and an occasional foreign body giant cell; *b*, solitary fibrous xanthoma, following trauma to extensor surface, showing foam cells; *c*, xanthoma involving tendon sheath, with replacement by foam cells.

changes, with infiltration of polymorphonuclear leukocytes and destruction of the foam cells resulting therefrom (fig. 7). Smith[45] has reported a case of xanthoma diabeticorum in which there were purpuric and ulcerating lesions differing only in degree from those of necrobiosis lipoidica diabeticorum. In one of our cases ulcerated and necrotic lesions were present. In most of the nine cases diabetes mellitus was of grade 3 or 4 severity. There was a family history of diabetes in two cases. Lipaemia retinalis was present in four cases and in each case responded to treatment.

The lesions of xanthoma diabeticorum are usually of the small fine papular type that are indistinguishable clinically from those of disseminate xanthomatosis without diabetes, but the extensor surfaces

TABLE 5.—*Xanthoma Diabeticorum*

Case	Age, Yr.	Sex	Duration of Diabetes, Yr.	Duration of Xanthoma, Mo.	Cholesterol, Cholesterol, Mg. per 100 Cc.	Cholesterol, Percentage of Total Lipoids	Lecithin, Mg. per 100 Cc.	Lecithin, Percentage of Total Lipoids*	Fatty Acids, Mg. per 100 Cc.	Total Lipoids, Mg. per 100 Cc.
1	35	M	1½	?	809	18	...	..	.....	5,037
2	27	M	½	4½	893	21	...	..	3,303	4,255
					665†	36†	...	..	1,189†	1,855†
					5‡	33	4‡	26	10‡	15‡
3	30	M	3	10	1,316	28	...	..	3,425	4,741
					653†	43†	...	..	847†	1,500†
4	50	M	2½	?	416	35	390	34	779	1,195
5	23	M	1	3	952	14	1,110	17	5,633	6,585
					505†	49†	398†	39†	515†	1,020†

* Calculated as percentage of total lipoids but included in fatty acids.
† After insulin and diet.
‡ Percentage of wet weight of tissue.

are commonly involved. There is a marked tendency for the palms and the soles to be involved by a diffuse, yellowish coloring (carotenosis), as well as by small nodular lesions.

Studies of the blood were made by the older methods of analysis in three of the cases. In two of these cases there was an elevation of the total lipoid and of the cholesterol content, and in the third the lecithin content was tremendously increased.

No cases of necrobiosis lipoidica diabeticorum (Urbach), as recently described in this country,[46] are included in this study. It would seem

45. Smith, J. F.: Xanthoma Diabeticorum with Purpuric and Ulcerating Lesions, Brit. J. Dermat. **46**:223-225 (May) 1934.

46. (*a*) Greenwood, A. M., and Rockwood, Ethel M.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **35**:727-729 (April) 1937. (*b*) Michelson, H. E., and Laymon, C. W.: Necrobiosis Lipoidica Diabeticorum (Urbach): Dermatitis Atrophicans Lipoides Diabetica (Oppenheim), J. A. M. A. **103**:163-169 (July 21) 1934.

that in this condition the greater part of the cholesterol is in a free rather than a combined form.[23] There is apparently a marked decrease in the amount of phosphatides (lecithin).

LIPOID PROTEINOSIS (LIPOIDOSIS CUTIS ET MUCOSAE)

This condition presents a definite clinical as well as pathologic appearance, which has been confirmed by recent articles in the literature.[47] We have yet to observe a case of it. The lesions of the mucous membranes must be distinguished from those of disseminated xanthomatosis.

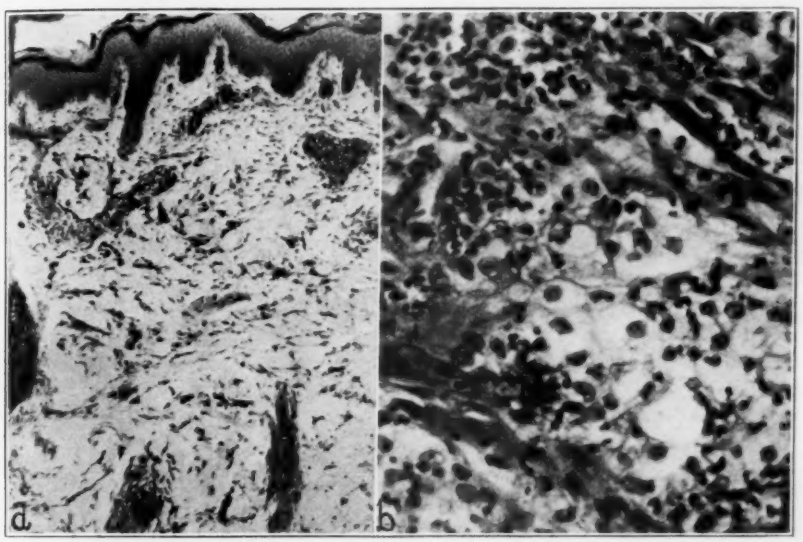

Fig. 7.—Xanthoma diabeticorum: *a*, deposits of lipoids, staining black, both intracellularly and extracellularly, outlining the reticulo-endothelial system; *b*, early stage of involution, showing invasion of xanthoma cells by polymorphonuclear leukocytic infiltrate.

XANTHOMA PALPEBRARUM

In the group of thirty-eight cases of xanthelasma histologic studies were made in seventeen cases and studies of the blood lipoids in nine. All but six of the thirty-eight patients had general physical examinations. Two patients showed hypertension, one with diffuse arterial

47. (*a*) Tripp, R. N.: Lipoidosis Cutis et Mucosae, New York State J. Med. **36**:619-626 (April 15) 1936; abstr., Wise, F., and Sulzberger, M.: Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1936, p. 270. (*b*) Wise, Fred: Lipoidosis Cutis et Mucosae, Arch. Dermat. & Syph. **35**:357-358 (Feb.) 1937. (*c*) Urbach.[5]

disease. Three had angina pectoris and coronary sclerosis, and one of these also had diffuse arterial disease, hypertension and diabetes. Thus, five of the thirty-two patients with xanthoma of the eyelids alone had serious disease of the cardiovascular system. Table 6 shows a definite increase in one or more of the lipoids in the blood and a consistent increase in the lecithin. Only in case 9 could the high value for cholesterol be explained on the basis of the patient's general condition, namely, as the result of a low basal metabolic rate not associated with myxedema;[48] yet, after thyroid medication had improved this condition, the cholesterol content had increased to 347 mg. per hundred cubic centimeters of plasma. The lipoids in the blood in xanthoma palpebrarum are not elevated as markedly as in xanthoma tuberosum, and

TABLE 6.—*Xanthoma Palpebrarum*

Case	Age, Yr.	Sex	Other Findings	Cholesterol, Mg. per 100 Cc.	Cholesterol, Percentage of Total Lipoids	Lecithin, Mg. per 100 Cc. of Plasma	Fatty Acids, Mg. per 100 Cc. of Plasma	Total Lipoids, Mg. per 100 Cc. of Plasma
1	50	F	Asthma	416	51	...	392	808
2	56	M	Rheumatic endocarditis, obesity (grade 2)	362	39	374	556	918
3	51	F	Obesity (grade 1)	303	40	...	444	747
4	60	M	Claudication, diabetes, angina pectoris	264	40	...	400	664
5	42	F	Secondary anemia	260	51	255	250	510
6	70	F	Pruritus ani et vulvae, obesity (grade 2)	238	35	305	435	673
7	45	F	None	219	38	328	356	575
8	53	F	Arthritis	203	33	348	412	615
9	49	F	Basal metabolic rate low (—18 per cent)	277	(347 after thyroid medication)			

there have been many cases in which the lipoids have been within normal limits.[10]

The histopathologic changes in xanthoma palpebrarum are similar to those in xanthoma in general, and include all stages from typical xanthoma to fibrotic changes. As a rule, relatively few Touton giant cells have been seen, and they have even been absent. There was a definite increase in the lattice fibers *(Gitterfäsern)* lying between and surrounding the xanthoma cells. There was no evidence of degenerative xanthomatous changes in the muscle fibers, as Pollitzer[49] once suggested. Anelli[50] has suggested that the lesions are based on a

48. Berkman, J. M.: Low Basal Metabolic Rate and the Use of Desiccated Thyroid, J. A. M. A. **106**:2042-2046 (June 13) 1936.

49. Pollitzer, S.: The Nature of Eyelid Xanthoma, J. Cutan. Dis. **28**:633-643 (Dec.) 1910. Pollitzer, S., and Wile, U. J.: Xanthoma Tuberosum Multiplex, ibid. **30**:235-241 (May) 1912.

50. Anelli, Dante: Sullo xanthelasma, Boll. d'ocul. **15**:263-278, 1936; abstr., Zentralbl. f. d. ges. Ophth. **36**:498, 1936.

neurovascular change. Sézary, Lichtwitz and Leblanc[51] reported the association of xanthomatosis and gouty tophi. The finding of xanthoma palpebrarum in more than 25 per cent of our cases of xanthoma tuberosum and disseminate xanthoma, together with the histologic picture and hyperlipemia, strongly suggests that xanthoma palpebrarum is an accompaniment of systemic disease and that the condition is simply a variation of one of the types of xanthoma.

SYSTEMIC DISEASE IN CUTANEOUS XANTHOMA

Evidence of severe damage to the liver was seen in five of the fifty cases and renal disease in three. Disturbances in hepatic metabolism have frequently been offered in explanation of cutaneous xanthoma.[52] In three of the four cases of disseminate xanthomatosis there was definite but mild diabetes insipidus, xanthomatous deposits in one case being found in the hypophysis and in the tuber cinereum at autopsy. Some authors have expressed the belief that the pituitary gland plays a definite and even active role in certain cases of abnormal lipoid metabolism.[53]

Of more importance, we feel, because it has not been emphasized in the literature, are the cardiovascular findings. There were seven cases of coronary sclerosis and angina pectoris and seven cases of other severe types of cardiovascular involvement, including four of intermittent claudication. In other words, a total of 28 per cent of the entire series of patients had cardiovascular disease.

All seven cases of coronary sclerosis and angina pectoris belonged among the twenty-six cases of xanthoma tuberosum. In four of the seven cases in which the blood was analyzed the value for cholesterol ranged from 438 to 672 mg. per hundred cubic centimeters of plasma, and the percentage of cholesterol in the total lipoids varied from 23 per cent (case 1) to 45 per cent. In three of these cases there was a family history of xanthoma. The average age of the twenty-six patients was 46 years, and the average age of the seven patients with coronary sclerosis at the time the diagnosis was made at the clinic was 47 years. Thus 27 per cent of the patients with xanthoma tuberosum had coronary sclerosis (one of these also had intermittent claudication). These

51. Sézary; Lichtwitz, and Leblanc, M.: Xanthome palpébral et auriculaire: Ses rapports avec l'hypercholestérinémie et l'hyperuricémie, Bull. Soc. franç. de dermat. et syph. **34**:7-11 (Jan.) 1927.

52. Brandt.[30a] Chaikoff, McGavack and Kaplan.[2a] Kyrle.[2b] McGavack and Shepardson.[2c] Schilling.[2d]

53. McGavack and Shepardson.[2c] Rowland.[3a] Weidman.[3b] Weidman and Schaffer.[3c]

figures more than triple those of Smith [54] for coronary disease in this age group. There was a high value for cholesterol in all seventeen of the twenty-six cases in which chemical studies were made, the amount varying from 303 to 672 mg. per hundred cubic centimeters of plasma. Five of the seven patients with other forms of cardiovascular disease were among those with xanthoma tuberosum, including three who had intermittent claudication, one with marked essential arterial hypertension and one with attacks of paroxysmal tachycardia. Three of the four patients with intermittent claudication (none of whom were Jews) and three of the seven with angina pectoris and coronary sclerosis were women, which is in contrast to the usual predominance in men. This increases the significance of these figures and indicates that a disturbance in cholesterol metabolism and an increase in total lipoids may play a definite etiologic role in angina pectoris and other severe cardiovascular disease. Of the twenty-six patients with xanthoma tuberosum, twelve, or 46 per cent, had severe cardiovascular disease.

Leary [55] has been able to reproduce the lesions of coronary sclerosis in rabbits by a suitable high fat diet. Mention should be made of the fact, pointed out by Schönheimer, that rabbits are not able to excrete cholesterol. Further evidence of a close relation between cutaneous xanthoma and cardiovascular disease is given in the frequent references in the literature to cardiovascular disease in association with juvenile xanthoma. Plewes [56] maintained that the xanthoma cell and the foam cell of atheroma are identical and that both arise from the reticuloendothelial system in response to the action of certain lipoids, especially cholesterol and its esters, when conditions favorable for their deposition in tissues are present. In view of the evidence just given, further investigation of the lipoid chemistry in angina pectoris and coronary sclerosis, especially in the early age groups, is being carried out.

ETIOLOGY OF XANTHOMA

The chemistry of cholesterol has recently been reviewed by Thannhauser,[57] and the theories regarding the etiology of xanthoma

54. Smith, H. L.: Incidence of Coronary Sclerosis Among Physicians as Compared with Members of Other Occupations, J. A. M. A. **108**:1327-1329 (April 17) 1937.

55. Leary, Timothy: Experimental Atherosclerosis in the Rabbit Compared with Human (Coronary) Atherosclerosis, Arch. Path. **17**:453-492 (April) 1934.

56. Plewes, L. W.: Nature and Origin of the Xanthoma Cell, Arch. Path. **17**:177-186 (Feb.) 1934.

57. (*a*) Thannhauser, S. J.: Ueber die Kostverordnung bei Lebererkrankungen und die diätetische Behandlung der Krankheitszustände mit Hypercholesterinämie, Schweiz. med. Wchnschr. **65**:1177-1181 (Dec. 7) 1935. (*b*) Thannhauser, S. J., and Magendantz, H.: The Differential Clinical Groups of Xanthomatosis Diseases, Ann. Int. Med., to be published.

have been discussed,[58] including that of the productive and that of the passive participation of the reticulo-endothelial system. It does not seem logical to us to explain the hyperlipemia and the hypercholesteremia in xanthoma tuberosum by the production of lipoids from the relatively few cutaneous xanthomatous nodules seen in this condition. This is like trying to explain the presence of uric acid in the blood as the result of the metabolism of uric acid in the gouty tophi present. Our experience coincides with that of Polano, in that in practically all cases of xanthoma tuberosum reported in the literature, and in all our cases there was an increase in the cholesterol and in the total lipoids in the blood, the cholesterol esters (combined cholesterol) predominating even in cases in which a moderate degree of hepatic damage was present. In disseminate xanthomatosis, on the other hand, there is no appreciable increase in the lipoids in the blood. This might be explained on the basis of a phenomenon of storage by the reticulo-endothelial system in the numerous cutaneous lesions present, but such an explanation would eliminate the possibility that cutaneous xanthoma itself is responsible for any increase in blood lipoids. Bloch[1a] and Schaaf[59] attributed xanthoma to an imbalance between the various lipoids, which in many cases is consistent with our chemical studies of tissue and blood. In other cases, however, there is a uniform increase in all the lipoids. There are many conditions associated with hyperlipemia in which no cutaneous xanthoma is present.[60] Many authors have shown that severe hepatic damage results in an increase in free cholesterol and a decrease in cholesterol esters in the blood.[61] Disturbances in vitamins, the participation of the pons or of the pituitary body in lipoid metabolism and the origin of xanthoma from the outer cells of the cutaneous nerve sheaths have been considered as etiologic factors.[62] In Weidman and Freeman's case both the pituitary body

58. (*a*) Gaines, M. T.: Xanthomatosis with Report of Case, South. M. J. **26**:489-496 (June) 1933. (*b*) Gruenfeld, Gerhard, and Seelig, M. G.: The Nature of So-Called Xanthoma, Arch. Path. **17**:546-573 (April) 1934 (*c*) McGavack and Shepardson.[2c] (*d*) Rowland.[3a]

59. Schaaf, Fritz: Weiterer Beitrag zur Pathogenese der Xanthome, Arch. f. Dermat. u. Syph. **163**:58-60, 1931. Schaaf.[15] Schaaf and Werner.[1b]

60. Ochsner, H. C., and Conner, H. M.: Lipemia Accompanied by Atheromatous and Occlusive Vascular Disease: Report of a Case and Partial Review of the Literature, Ann. Int. Med. **10**:258-269 (Aug.) 1936. Gruenfeld and Seelig.[58b] Polano.[10] Wile, Eckstein and Curtis.[20b]

61. (*a*) Hübner, K. H.: Zur Chemie des Leberstoffwechsels bei Infiltrationsxanthelasmen, Arch. f. Dermat. u. Syph. **171**:571-576, 1935. (*b*) Laroche, Guy; Grigaut, A., and Costes: Les variations du rapport des esters du cholestérol au cholestérol total en pathologie, Presse méd. **42**:1417-1419 (Sept. 12) 1934. (*c*) Thannhauser and Magendantz.[57b]

62. Weidman.[3b] Weidman and Schaffer.[3c]

and the liver might be considered to have played etiologic roles. Retention of cholesterol in the body, emphasized by Schönheimer, and the reduction and even the disappearance of cutaneous lesions of xanthoma tuberosum following administration of a diet low in cholesterol and free from animal fat—which, however, is said not always to occur [63]—do not account for the persistence of lesions of disseminate xanthomatosis with the same type of diet. This is especailly true in view of the normal or low values for lipoids in the blood in disseminate xanthomatosis. Our observations are in accord with those of Wile, that lipoids in blood and in tissue do not correspond in the same case. In all our cases there was a marked increase in the cholesterol content of the xanthomatous nodules, except when marked evidence of fibrosis was seen histologically. This is in disagreement with Eckstein and Wile's earlier findings [21] but corresponds to their later observations.[20a] Urbach has made a valuable contribution in separating various types of xanthomatosis on the basis of the predominance of one type of lipoid over another. In all our fifty cases, however, there was a disturbance, usually in cholesterol metabolism, and in only a few cases was there any marked increase in lecithin in either blood or tissue. Weidman [64] has aptly stated that probably there are many forms of lipoids that remain unknown. The older etiologic concept that an excess of cholesterol is responsible for the production of xanthoma must still be considered. Trauma and infection in our experience have played minor roles. No one of the current theories, however, satisfactorily explains all instances of cutaneous xanthoma. The etiology of xanthoma, therefore, still remains unknown.

DIFFERENTIAL DIAGNOSIS

The histologic picture of an early or well developed nodule of xanthoma is typical and diagnostic and consists of many foam or xanthoma cells in intimate relationship with capillaries and smaller blood vessels in the upper part of the cutis, frequently with a varying number of so-called Touton giant cells and occasionally with some foreign body giant cells. The number of lattice fibers (*Gitterfäsern*) is increased. No evidence of any change in the cutaneous nerves was observed. In the stages of involution and fibrous change the histologic picture closely approximates that of dermatofibroma. In both there are few xanthoma cells, much extracellular deposit of lipoids of different

63. Sperry, W. M., and Schick, Béla: Essential Xanthomatosis: Treatment with Cholesterol-Free Diet in Two Cases, Am. J. Dis. Child. **51**:1372-1384 (June) 1936.

64. Weidman, F. D.: Studies in Hypercholesterolemia: III. The Approach to the Pathogenesis of the Xanthomas, Arch. Dermat. & Syph. **15**:659-668 (June) 1927.

types and deposits of hemosiderin. With a solitary lesion, there is an increase in lattice fibers in *Gitterfäsern* and distinction between the two conditions may be impossible. In two of the three instances of clinical dermatofibroma lenticulare (histiocytoma) there were a definite elevation of the cholesterol and total lipoid contents of the blood and an increase in various lipoids in a nodule, the findings paralleling those for xanthomatous nodules. An increase in cholesterol in the blood has been reported in cases of so-called xanthic tumors of the tendon sheaths.[65] Histopathologically, these tumors show a varying number of xanthoma cells, considerable cholesterol and other lipoids deposited intracellularly and extracellularly, many foreign body giant cells and occasional Touton and endothelial types of giant cells.[66] In none of the thirteen cases in which histologic studies were made was there any evidence or history of subsequent malignant change. The evidence given in recent articles in the literature is against the old concept that xanthosarcoma arises from xanthic lesions of the tendon sheaths or xanthoma elsewhere in the body.[67]

Just as foam cells may be encountered histologically in other conditions, as in association with fatty changes in true neoplasms of various types, in chronic systemic diseases and in inflammatory dermatoses, so does one find instances of marked hyperlipemia of all the various lipoids in the blood in many cases in which there is no evidence of cutaneous xanthoma.[69] Thus hyperlipemia is seen, for example, in some cases of general atherosclerosis and nephrosis, of marked hepatic disease and of tuberculosis, leukemia and myxedema.

Differentiation of juvenile xanthoma from urticaria pigmentosa may be made on the basis of the concomitant findings. The same is true of parapsoriasis and lipoid degeneration of the elastic tissue, as described by Urbach [5] and Weidman.[68] Pseudoxanthoma elasticum morphologically and histologically has nothing in common with cutaneous xanthoma, and the same is true of ganglioneuroma of the skin [69] and so-called Danlos' syndrome.[70]

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65. Zumtobel, M.: Beitrag zur Klinik und Pathologie der gutartigen Sehnenscheidentumoren mit besonderer Berücksichtigung der xanthomatösen Riesenzellengeschwülste, Deutsche Ztschr. f. Chir. **247**:501-516, 1936.

66. Broders, A. C.: Benign Xanthic Extraperiosteal Tumor of the Extremities Containing Foreign Body Giant Cells, Ann. Surg. **70**:574-581 (Nov.) 1919.

67. Geschickter, C. F.: Lipoid Tumors, Am. J. Cancer **21**:617-641 (July) 1934. Weidman and Schaffer.[3c]

68. Weidman, F. D.: The Pathology of the Yellowing Dermatoses: I. Non-xanthomatous (Jaundice, Carotinemia, Blood Pigmentation, Melanin, Colloid Degeneration, and Elastic Degeneration), Arch. Dermat. & Syph. **24**:954-991 (Dec.) 1931. Weidman and Schaffer.[3c]

69. Montgomery, Hamilton, and O'Leary, P. A.: Multiple Ganglio-Neuromas of the Skin: Report of a Case with Differential Diagnosis from Reticulohistiocytic

(Footnotes continued on next page)

SUMMARY AND CONCLUSIONS

It is important to distinguish between the different types of cutaneous xanthoma because of the variations in prognosis and response to treatment. Xanthoma tuberosum can usually be distinguished from disseminate forms of cutaneous xanthomatosis.

Xanthoma tuberosum is usually associated with a high value for cholesterol in the blood and an increase in total lipoids. Severe cardiovascular damage, especially coronary sclerosis and intermittant claudication, is frequently found. In disseminate xanthomatosis there is a high incidence of diabetes insipidus; the contents of lipoids in the blood as a rule are within normal limits, and no involution of the lesions ordinarily occurs during any dietary regimen. In xanthoma tuberosum the lesions may undergo partial or complete involution, and the lipoids can be brought to normal by a low caloric reducing diet or one free from animal fat (hence low in cholesterol). The results of chemical analysis of material from the xanthomatous lesions do not parallel those of the blood. In both xanthoma tuberosum and disseminate xanthomatosis there is a definite proportionate increase in the cholesterol content except in old fibrous lesions, which histologically reveal few foam cells. The amount of cholesterol esters exceeds that of free cholesterol.

Juvenile xanthoma may occur, usually in the tuberous and occasionally in the disseminate form. Cardiovascular lesions have frequently been reported. There ordinarily is an increase in one or more or all of the lipoids in the blood.

Xanthoma palpebrarum is frequently seen in association with other forms of xanthoma of the skin. Even in a series of cases in which xanthoma was limited to the eyelids evidence of varying degrees of hyperlipemia and of systemic disease was not infrequently encountered.

Nevoxantho-endothelioma belongs to the group of xanthoma rather than to that of endothelioma, and it may be distinguished by the distinctive histologic picture, by the absence of hyperlipemia and by the history of spontaneous involution of the lesions.

Xanthoma diabeticorum in our experience is seen in cases of severe diabetes associated with chronic acidosis and marked hyperlipemia, and the lesions almost invariably undergo involution when dietary restrictions and insulin therapy are instituted. Lipoids may be found by histologic examination extracellularly as well as intracellularly, especially in lesions in the process of involution.

It is questionable whether "extracellular cholesterosis" (Urbach) should be classified as a separate type of xanthoma. It may be

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Granuloma, Neuroma, Xanthoma and von Recklinghausen's Disease of the Skin, Arch. Dermat. & Syph. **29**:26-52 (Jan.) 1934.

70. Tobias, Norman: Danlos Syndrome Associated with Congenital Lipomatosis, Arch. Dermat. & Syph. **30**:540-551 (Oct.) 1934.

impossible to distinguish between the histologic picture of dermatofibroma (histiocytoma) and that of the solitary fibrous stage of xanthoma. Various theories regarding xanthomatosis are mentioned, but none of them at present offer a satisfactory explanation of all types of xanthoma.

ABSTRACT OF DISCUSSION

Dr. Herman Sharlit, New York: I had the pleasure yesterday afternoon of reading Dr. Montgomery's manuscript, with its wealth of data, clinical, histologic and biochemical. I want to limit my comments to a few of the thought-provoking features of his biochemical findings and to begin them by congratulating the author on the realization, in reporting his studies, of the necessity for indicating the analytic technics used and for stating explicitly that samples for analysis were taken early in the morning, before the subject had breakfasted. The critical reader of quantitative studies in dynamic physiology must know the nature of the instruments used in measuring and must know that in the taking of samples for analysis precautions were taken to minimize the influence on these measurements of ingested foodstuffs.

The lipoids are a group of heterogeneous units bound together by the common physical properties of solubility in solvents of the type of alcohol, ether and acetone and by their immiscibility with water. Yet living protoplasm must achieve for these lipoids a miscibility with water, life's common denominator. In physiochemical terminology one may define protoplasm as an emulsion of oil in water and of water in oil. Without burdening the members with evidences of the importance of cholesterol in the production of these emulsifications, I want simply to recall the ease with which grease can be hydrated by the incorporation therein of oxy-derivatives of cholesterol. It would appear that free cholesterol and possibly its esters are deeply concerned in the mechanism of making protoplasm hydrophilic. One can therefore appreciate the significance of a disturbance in hydrous metabolism accompanied with evidences of faulty deposition of cholesterol in tissues, as in Schüller-Christian disease. Until yesterday I knew of no reported case, other than those of the Schüller-Christian syndrome, in which cholesterol deposits were associated with diabetes insipidus. Yet Montgomery has made the astonishing revelation that in all four of his cases of disseminate xanthomatosis diabetes insipidus complicated the picture—two clinical pictures, each relatively uncommon in its own right, meeting in one patient in four successive instances. Biologic statisticians will say that that spells relationship unequivocally. If these cases are not instances of Schüller-Christian disease, they represent clinical evidence of a new variety demonstrating the relationship of the metabolism of cholesterol and of water, a relationship mediated through pituitary hormones. I trust that dermatologists will continue to delve into the subject of this relationship.

Much as I should like to comment on the total and ratio measures of the several lipoid fractions reported and on the relationship of the hyperlipemia to lipoid deposits in the skin, time forbids this. I have privately given to Dr. Montgomery my objections to the use of wet weight figures in analyses of tissue, and I have indicated to him a practical procedure for preliminary dehydration of tissues. I congratulate him and sincerely trust he has hit on a clue that may be productive of yet another bit of truth.

Dr. Hamlton Montgomery, Rochester, Minn.: I wish to thank Dr. Sharlit for his discussion and for his suggestions. None of the cases of disseminate xanthomatosis were those of children, and in none was there any demonstrable

evidence of Hand-Schüller-Christian disease. The roentgenograms of the head and the other bones showed no abnormality, and there was no evidence of exophthalmos or other symptoms of Hand-Schüller-Christian disease. Chemical analysis based on the wet weight of the xanthomatous nodules would result in an increase in the percentage of total lipoids if the tissue had been allowed to dry out before being weighed but would not affect the percentage ratio between the various lipoids. We used this method of analysis because it had been employed by others, and we wished to make comparative studies.

The case presented in connection with this paper but not included in the fifty cases, which could be classified as one of hepatosplenomegaly of Bürger and Grütz with lipoidosis of the skin and mucous membrane, will be reported later. It is of significance in the etiology of xanthoma, because the hepatic changes preceded any cutaneous xanthoma by many years. This emphasizes the prominent part that the liver may play in lipoid disturbances in many instances; furthermore, when there is severe hepatic damage the ratio between free and combined cholesterol is reversed, the free cholesterol predominating. The marked increase in the phosphatide lecithin in the blood distinguishes these cases from others that I have seen in which xanthoma appeared secondarily to biliary cirrhosis but in which the normal ratio of the various lipoids in the blood was preserved in spite of an increase in the total lipoids. In Weidman and Freeman's case, now classified as one of Hand-Schüller-Christian disease, the patient presented lesions of both disseminate and tuberous xanthoma after evidence of disease of the liver and the pituitary gland. In this instance both organs probably play a part in the etiology, and hypercholesteremia could be explained by the disease of the liver. I am beginning to think, therefore, that the etiology of xanthoma must be explained by multiple factors which vary in individual cases, the tuber cinereum and the pituitary gland or the liver playing a prominent role in certain instances, while in many cases of xanthoma tuberosum accompanied with hypercholesteremia and hyperlipemia a source of the increase in the lipoids in the blood remains to be found.

Dr. Weidman referred to the relation of juvenile xanthomatosis to nevi and the possible origin of xanthoma in the nerve sheaths. In none of this series was I able to demonstrate any changes in the cutaneous nerves with either the Van Gieson or the Maersh-Bielschowsky stain. May I emphasize in closing that in ordinary xanthoma tuberosum, with or without hepatic disease, there is hypercholesteremia, whereas in disseminate xanthomatosis, with multiple, small lesions predominating on the flexural surfaces and the mucous membranes, the lipoids in the blood remain within normal limits? In xanthoma tuberosum there is a high incidence of cardiovascular disease, and in disseminate xanthomatosis there is frequently associated diabetes insipidus.

LUPUS ERYTHEMATOSUS

INCREASED INCIDENCE, HEMATOPORPHYRINURIA AND SPECTROSCOPIC FINDINGS

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In recent years the literature on lupus erythematosus has increased decidedly, the disease now occupying a place second to syphilis in the number of contributions to dermatologic publications. Since 1924 attention has been given especially to treatment. More recently, however, as the novelty and variations of therapy subsided and further experience checked early enthusiasm, some physicians in Philadelphia had their attention diverted to the marked increase in incidence of the disease. The number of new cases in recent years would lead to the belief that there is justification for concluding that a virtual epidemic of this malady is present.

At the Hospital of the Protestant Episcopal Church only 6 new cases of lupus erythematosus of all types were listed during 1930, a year in which 830 new cases of cutaneous disease were observed, making an incidence of 0.72 per cent. Until that time the number of cases of lupus erythematosus had never reached that figure in any year. From 1930 on the increase has been steady. In the first four months of 1937 there have been 20 cases, which would mean 60 cases for this year if that rate were sustained. As the number of new cases has steadily increased during the last seven years, our records show that for the past five years cases of lupus erythematosus have topped the 2 per cent mark among new cases of cutaneous disease, reaching the high figure of 2.67 per cent in 1936.

In a survey of diagnoses covering the ten years from 1920 to 1931 in private practice lupus erythematosus occupied the twenty-fourth place, with a percentage of 0.76 per cent. Had this been 2.67 per cent, as in 1936, the disease would stand eleventh in this ten year period. Thus it would seem that a condition formerly classed by Macleod as

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"one of the more common of the rarer dermatoses" [1] has become decidedly more common.

As our experience at the Hospital of the Protestant Episcopal Church did not agree with that of other clinics in the service, we at one time considered the possibility of a regional outbreak in a certain quarter of the city. This hospital is located in a district where factories are abundant, most of them being textile plants, which are served for the most part by workers of Anglo-Saxon stock. We followed up this increase in incidence by plotting on the map of the city the addresses of some 150 patients from several institutions. Although the highest incidence naturally was in the region surrounding each hospital, there was, in a diminishing scale, such a uniform representation from more distant sections of the city and suburbs that it was felt that the hypothesis of a regional outbreak could not be held.

With an abundance of material it was but natural that a desire for a more definite understanding of the etiology should ensue. In accord

Figures Showing Increased Percentage of Lupus Erythematosus

	1915	1930	1931	1932	1933	1934	1935	1936
New cases of cutaneous disease.....	627	830	980	1165	1190	1210	1590	1835
New cases of lupus erythematosus..	0	6	10	24	29	30	32	49
Percentage	0	0.72	1.02	2.06	2.43	2.47	2.01	2.67

with some of the reports of autopsies [2] already published, our findings revealed that the presence of tuberculosis cannot always be proved in patients with this disease. Nevertheless, the association of lupus vulgaris and other forms of undoubted cutaneous tuberculosis [3] with lupus erythematosus occurs frequently enough not to be entirely disregarded. The majority of European observers and those in the Argentine [4] are of the opinion that the disease has a tuberculous background. An investigation of 200 cases observed by us before Dec. 31, 1936, showed

1. Macleod, J. M. H.: The Etiology of Lupus Erythematosus, Arch. Dermat. & Syph. **9**:1 (Jan.) 1924.

2. Garfield, W. T.; Steele, C. W., and Houghton, J. D.: Lupus Erythematosus Disseminatus Acutus Haemorrhagicus, Arch. Dermat. & Syph. **30**:772 (Dec.) 1934.

3. Montgomery, D. W.: Coincidence of Lichen Scrofulosorum with Lupus Erythematosus, Arch. Dermat. & Syph. **31**:37 (March) 1935. Parounagian, M. B.: Lupus Vulgaris and Lupus Erythematosus, ibid. **31**:419 (March) 1935. Gaté, J.; Cuilleret, P., and Recent, L. E.: Papulonecrotic Tuberculides of Scalp, Bull. Soc. franç. de dermat. et syph. **41**:580 (April) 1934.

4. Pessano, J.: Clinical Forms and Therapeusis of Lupus Erythematosus, Rev. argent. de dermat.-sif. **16**:158 (Nov.) 1933.

only 14 in which tuberculosis appeared on clinical examination, roentgenologic study, analysis of sputum or autopsy. In 5 there was cutaneous tuberculosis, taking the form of lupus vulgaris, in 2 cases, of scrofuloderma in 1 and of papulonecrotic tuberculid in 2. Only 2 cases were reported in which the sputum gave a positive reaction on examination for tubercle bacilli.

Studies of the blood revealed the commonly encountered leukopenia, so well exemplified by Hollander and his associates,[5] Mook and his associates[6] and numerous others, and the increased lymphocytic index in differential counts. Frequently the lymphocytic increase appeared to be relative, because it seemed an exaggeration resulting from a diminished number of polymorphonuclear leukocytes. However, in some cases in which the white blood cell count was within normal limits there were lymphocytic percentages ranging around 40. Lymphocytosis is apparently a symptom of exposure to the short ultraviolet rays.[7]

The rôle of vitiligo is not clearly understood. The term has been used by some observers to describe a clinical form of lupus erythematosus. Many clinicians, especially those in Europe, have stated that they consider vitiligo an evidence of sensitivity to light.[8]

We have not found hematoporphyrin in vitiligo but have frequently observed the presence of leukopenia and lymphocytosis in patients with that condition. In one patient with vitiligo a careful check-up showed a leukocyte count of 8,000, with a lymphocyte count of 70 per cent repeatedly evident. For this we have no explanation to offer.

Urinalysis, particularly in cases of the acute disseminated type of lupus erythematosus, showed a definite high incidence of hematoporphyrin, a manifestation which led us to believe that the light factor and the presence of this photosensitizing agent in the blood might account for the production of the cutaneous lesions. Of the 200 cases cited here, 18 (9 per cent) were of the acute or subacute disseminated type. Nine of the patients in that group are known to be dead. In 4 of the fatal cases and in 3 of those in which the patient survived, hematoporphyrin was found in the urine in abnormal quantities. The

5. Hollander, L.; Kastlin, G.; Fisher, A., and Schlesinger, Clara R.: Lupus Erythematosus Subacutus with an Unusual Blood Picture, Arch. Dermat. & Syph. **25**:353 (March) 1932.

6. Mook, W. H.; Weiss, R. S., and Bromberg, L. K.: Lupus Erythematosus Disseminatus, Arch. Dermat. & Syph. **24**:786 (Nov.) 1931.

7. Krusen, Frank H.: Light Therapy, ed. 2, New York, Paul B. Hoeber, Inc., 1937.

8. Kitchevatz, M.: Étiologie et pathogenèse de la dermatose striée photodermite actino-calorique chlorophyllienne, Ann. de dermat. et syph. **5**:293 (March) 1934.

examination was not carried out in 3 instances. In the remaining 8 the report was negative. Examination for hematoporphyrin in 27 cases of chronic lupus erythematosus of the fixed and disseminated types gave positive results in 10, in which without exception, there were signs of activity and progress. In the 3 cases of acute disseminated lupus erythematosus in which autopsy was performed hematoporphyrinuria was present before death. In addition, in each there was a clear history and a distribution of the eruption indicating exposure to light as one of the factors responsible for the outbreak. As a typical instance the following history is briefly outlined:

Case 1.—M. T., an Italian girl aged 19, well developed and apparently healthy, showed reddish dots on her nose on May 1, 1933. This outbreak followed exposure to sunlight. The spots increased in size, coalesced, and joined similar areas on the cheeks. New areas appeared on the fingers, the forearms and the shoulders. Whitish scales were first seen on July 5, and distinct margination of the patches was noted on the face. The differential blood count showed 51 per cent polymorphonuclear neutrophils and 49 per cent lymphocytes. The blood count showed 5,600 white cells, 3,320,000 red cells and 78 per cent hemoglobin. The patient was admitted to the Chestnut Hill Hospital for study on July 17. Her temperature ranged from 100.6 F. on admission to normal on discharge, July 25. Except for a report on the nose and throat advising tonsillectomy, no important information was gained during her stay in the ward. During the following fall and winter the condition improved markedly but did not entirely disappear. She never received injections of a gold compound and was not under the care of a dermatologist. About the middle of May 1934 fever began again, and the eruption reappeared in the former locations. The skin was bluish red, peeled and was sensitive to touch. By June 1 involvement of the palate and also of the buccal mucosa was noted. She was readmitted to the hospital June 25. From that time until her death, July 27, the course of the disease was that usual for a desperately ill patient with acute disseminated lupus erythematosus of a septicemic type. Cultures of the blood never gave positive results. Roentgen examination of her chest showed a slight increase in prominence of markings on the trunk to the apex of the left lung and multiple calcified elements in the right hilar region. The leukocytic count ranged from 3,750 to 7,000, with a lymphocytic count of approximately 48 per cent at all estimations. The urine showed a light cloud of albumin and hyaline and granular casts. The test for hematoporphyrin was conducted at the Lankenau Hospital. Two urinalyses showed hematoporphyrin during a twenty-four hour period. Of these, the morning specimen showed double the quantity of hematoporphyrin of the evening one. The sedimentation of the red blood cells was rapid, the rate being 37 mm. in twenty-five minutes. The teeth and gums showed no spirochetes or fusiform bacilli.

At autopsy there was no evidence of pulmonary tuberculosis, but diffuse bronchopneumonia existed, especially in the lower lobe of the right lung posteriorly. Evidences of acute and of chronic streptococcic infection were present in many organs. The pathologic report included mention of acute pericarditis and myocarditis, chronic pancreatitis and splenitis, acute fatty degeneration of the liver and chronic tubular nephritis with glomerular involvement. Enlarged lymph nodes encased the great vessels from the region of the spleen to that of the pancreas. On gross examination the intestines showed no abnormality.

For the sake of uniformity of technic examinations for hematoporphyrin were carried out at the laboratory of pathology of the Lankenau Hospital under the direction of Dr. Stanley P. Reimann. The results of the early chemical tests were confirmed by spectoscopic studies. Since the results of the two types of test appeared to correspond, chemical tests were eventually relied on by the pathologist in charge.

Hematoporphyrin is found in the urine in a number of pathologic conditions, among which lead poisoning [9] is to be mentioned.

The following case is reported to illustrate this phase of the study:

CASE 2.—M. H., a white woman, unmarried, aged 23, came to the outpatient department of the Hospital of the Protestant Episcopal Church in March 1934 because of a generalized eruption of nine months' duration. It had begun at the seashore the previous summer as typical butterfly patches on the cheeks and the nose with involvement of the neck and the décolletage both in front and in back. A similar outbreak appeared subsequently on the shoulders, the arms, the hands and the lower parts of the legs. General medical examination showed nothing of special interest bearing on the condition except three abscessed teeth, which were extracted. On admission to the hospital, July 20, 1934, examination of the blood gave the following results: 3,290,000 red cells, 4,800 white cells, 36 per cent lymphocytes and 420 mg. chlorides and 110 mg. sugar per hundred cubic centimeters. The sugar content fell in a few weeks to 84 mg. and the chlorides rose to 465 mg. per hundred cubic centimeters. Urinalysis showed no abnormality; the blood pressure was 104 systolic and 70 diastolic; the patient weighed 114 pounds (42.5 Kg.). After eight weeks' stay in the hospital there was some improvement, and on discharge the patient resumed work in a textile mill. Swift relapse followed, as a result of working under powerful illumination. On her admission to the Lankenau Hospital, March 27, 1935, the history revealed that she had previously worked for some time in a tinsel manufacturing plant. Hematoporphyrinuria was strongly evident. Spectrographic examination of an incinerated biopsy plug showed acute retention of lead. Two spectrographic examinations of tissue from this patient were performed by Dr. L. E. Gaul, of New York. Three transfusions of 50 cc. of whole blood were given from a typed donor who one hour previously had received an injection of 0.1 Gm. of sodium gold thiosulfate. The patient was placed on a metal-free diet with low calcium and high phosphorus contents, together with ammonium chloride medication. Improvement was steady, and at present there is no trace of the former lesions. Two biopsy plugs removed at intervals of six months and examined by means of the spectroscope have shown no lead. Hematoporphyrinuria has been absent in subsequent examinations.

Nontherapeutic electric lights have been known [10] to aggravate or produce lupus erythematosus. Further elaboration of this fact is unnecessary.

The finding of hematoporphyrin in this case stimulated further inquiry and accounted for its recognition in the urine of many patients

9. Hausmann, W.: Zur sensibilisierenden Wirkung der natürlichen Porphyrine, Biochem. Ztschr. **77**:268, 1916.

10. Bechet, P. E.: Treatment of Lupus Erythematosus with a Gold Preparation, Arch. Dermat. & Syph. **20**:257 (Aug.) 1929.

with acute or subacute lupus erythematosus. When these persons made progress the hematoporphyrin disappeared coincident with their improvement in other respects.

We believe, consequently, that the presence or absence of this substance is of prognostic importance somewhat akin to that of leukopenia, which is relatively ominous according to degree. Naturally, it has occurred to other observers to look for hematoporphyrin. Tulipan [11]

Fig. 1 (case 2).—Photograph taken during the height of the eruption, in May 1934.

mentioned his inability to find it. Goeckerman [12] did not find it in his patients. Brunsting and Nomland [13] reported the presence of hematoporphyrinuria in a girl 15 years of age with long-standing lupus erythematosus.

11. Tulipan, L., in discussion on Rosen, I.: Lupus Erythematosus, Arch. Dermat. & Syph. **23**:560 (March) 1931.

12. Goeckerman, W. H.: Personal communication to the authors.

13. Brunsting, L. A., and Nomland, R.: Lupus Erythematosus, Arch. Dermat. & Syph. **27**:1035 (June) 1933.

This photosensitizing agent may be present in traces not easily perceptible by tests in normal human urine. It is an intermediate factor of importance in the production of certain cutaneous diseases. The presence of hematoporphyrin is probably due to hepatic damage or insufficiency [14] or to some pathologic change in the bone marrow.[15]

Fig. 2 (case 2).—Present appearance of the patient (May 1937). The small spots are freckles.

We are venturing to add the mineral poison, lead, to the number of toxic agents already regarded as causal agents in producing lupus erythematosus.

14. Mathews, F. P.: Photosensitization and the Photodynamic Diseases, Arch. Path. **23**:406 (March) 1937.

15. Gray, A. M. H.: Haematoporphyria Congenita with Hydroa Vacciniforme and Hirsuties, Quart. J. Med. **19**:381, 1926.

Experience has shown that minimum quantities of heavy metals circulating in the blood considerably increase the effects of ultraviolet rays on the organism; conversely, the efficacy of the heavy metals is distinctly increased under the influence of ultraviolet radiation.[16]

Traub[17] exhibited a printer with disseminated lupus erythematosus who was possibly subject to saturnism.

It was decided to investigate the metallic content of the integument of a series of patients in order to throw more light on the matter. Interest in this phase of the subject was stimulated by the work of Gaul and Staud, especially their study in regard to the retention of nickel in psoriasis.[18]

Investigation has so far been completed in 41 instances. Of these, 18 subjects had lupus erythematosus. Twenty patients with no lupus erythematosus were employed as controls. The remaining 3 patients were sufferers from lead poisoning, in 1 of whom the condition was acute and in 2 chronic, without lupus erythematosus or other cutaneous manifestations.

Spectroscopic investigations for this study were carried out in the department of physics of the University of Pennsylvania. The source of light employed was the carbon arc, and by this means the analyst burned electrically the biologic specimen submitted to him for examination. Another method employed for this purpose is the high frequency spark gap. There are certain objections to both methods, and the margin of error in either is about 10 per cent.

In obtaining tissue the most important requirement is avoiding the use of any improper chemical reagent. All biopsy specimens were uniformly taken with a $\frac{3}{16}$ inch (0.47 cm.) punch from the same area on the front of the thigh of each patient. Each specimen was placed in a hollow carbon electrode and heated by the passage of a current through it. In this manner the specimen was rendered luminous. The control consisted of a standard solution of the element or elements in known amounts. The intensity of a given spectroscopic line in the control and the amount of the element in the tissue were compared. Lead acetate was employed in this investigation as the control salt.

Lead occurs in the tissues spasmodically. Its varied and irregular distribution strongly suggests that the metal is accidentally present. It is known that in cases of lead poisoning the element may be stored in

16. Sibley, W. Knowsley: The Treatment of Diseases of the Skin, ed. 4, London, Edward Arnold & Co., 1933, pp. 37-38.

17. Traub, E. F.: A Case for Diagnosis (Lupus Erythematosus Disseminatus?), Arch. Dermat. & Syph. **25**:562 (March) 1932.

18. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: The Quantitative Retention of Nickel in Psoriasis, Arch. Dermat. & Syph. **30**:697 (Nov.) 1934.

certain tissues. Fox and Ramage [19] stated that "we have found lead in three human subjects. The remarkable fact is that the lead was present in different organs in each man." It is evident that lead is

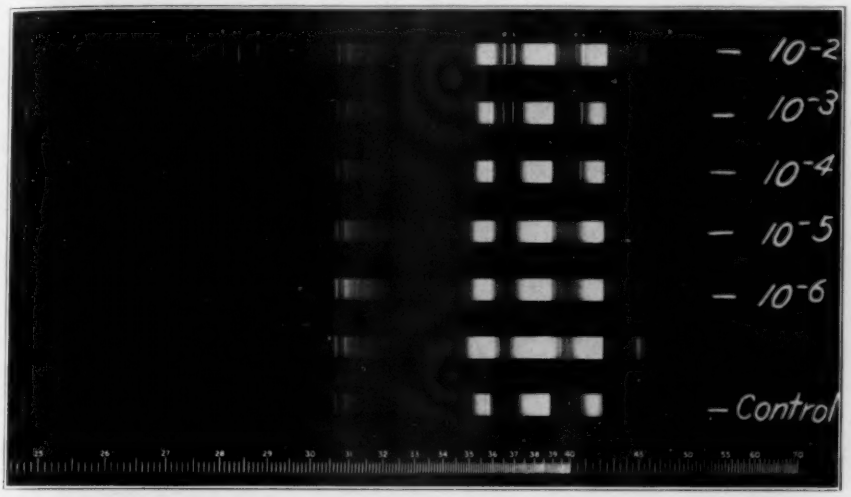

Fig. 3.—Spectrum of a standard lead preparation. The broad bands on the spectrum indicate cyanogen derived from the nitrogen in the air. Nearly all the other lines indicate iron (due to blood contamination). The line above the control is a pure carbon spectrum. Dots indicate lead lines at angstroms 4057.8; 3683.5, and 2833.1. The standard solution is formed by adding 1 Gm. of lead acetate to 100 cc. of triple distilled water. A 10 per cent solution of this standard preparation is represented by the line 10-2. Each successive decimal dilution is in order below.

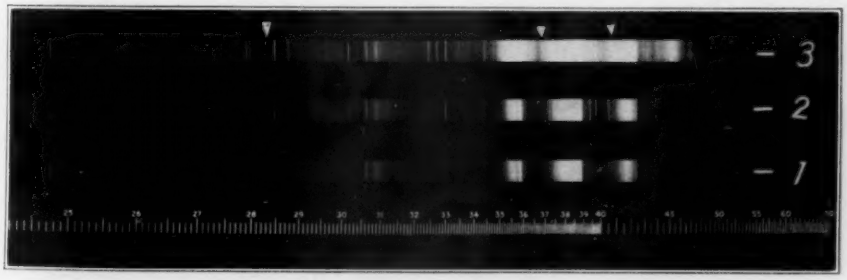

Fig. 4.—Spectrum of a specimen from a patient with lupus erythematosus. The pathologic amount of lead is indicated by pointers.

stored in the tissues whenever it is available and when tissues have an affinity for it.

19. Fox, H. Munro, and Ramage, Hugh: A Spectrographic Analysis of Animal Tissue, Proc. Roy. Soc., London, s.B **108**:157, 1931.

Spectrographic examination of a patient who died of lead poisoning demonstrated no lead in the spleen, the kidneys, the heart, the lungs, the pancreas, the lymph glands, the blood and the skin, while the liver and the intestines showed faint traces.[20]

Of the 18 cases of lupus erythematosus just mentioned, in 15 there was marked evidence of lead and in 3 faint evidence. Among the 20 control subjects 17 gave no evidence of lead; 1 showed a trace, and 2 showed small quantities. It is of interest to mention that the last 3 subjects had vitiligo. Vitiligo was not present in the other 17. The 3 patients with lead poisoning did not show the element in spectroscopic studies of the skin.

SUMMARY AND CONCLUSION

Careful observation of the incidence of lupus erythematosus in Philadelphia points to a decided increase during the last few years. While bacterial toxins seem to be well established factors in effecting organic and dermal changes, the possibility that metallic poisons produce similar changes must be considered.

Hematoporphyrin was noted in many patients with acute lupus erythematosus. This substance, acting as a photodynamic sensitizer, could readily account for dermal changes. Along with other danger signals, such as leukopenia, marked lymphocytosis and high sugar and low chloride contents of the blood, hematoporphyrinuria may take its place as a deterrent to the use of gold compounds in treating lupus erythematosus.

We propose that in a susceptible subject with, say a streptococcic toxemia or a cross-fire tuberculous-pyogenic background, the presence of a porphyrin substance in the blood stream may engender photosensitivity and cause lupus erythematosus to appear as a result of exposure to light. In some cases a metallic element acting as a catalyst may be responsible for producing the same result. It appears from our observations of a few cases of early lupus erythematosus that in all cases in which chronic discoid characteristics appear later there may have been a stage in which porphyrin was present. When the stationary stage is reached, porphyrin cannot be detected in abnormal quantities.

The presence of lead in the skin of every patient with lupus erythematosus that has been examined with the spectroscope seems more than coincidental and encourages us to continue investigating this aspect of the disease.

Spectroscopic studies were directed by Dr. Philip Q. Roche, whose findings were checked by Prof. C. B. Bazzoni, of the department of physics of the University of Pennsylvania.

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20. Gerlach, Walter, and Gerlach, Werner: Clinical and Pathological Applications of Spectrum Analysis, Berlin, Adam Hilger, Ltd., 1934, p. 75, line 18.

ABSTRACT OF DISCUSSION

DR. MAURICE MYER TOLMAN, Chelsea, Mass.: At the Massachusetts General Hospital I studied between January 1930 and December 1936 a series of 121 consecutive cases of lupus erythematosus discoides. The condition was treated with sodium gold thiosulfate, bismuth subsalicylate and calcium levulinate, and with each drug I found instances of cure, of excellent response, of improvement both great and slight, of failure and of recurrence.

I therefore was led to believe that these metals were acting as alteratives rather than in any specific manner.

The analysis of statistics as to age, sex and nativity revealed little; except in cases in which the employment was such as to necessitate considerable exposure to the sun, occupation seemed of little importance. In the series were representatives of 31 widely divergent types of employment.

There were but 7 cases in which there was a clinical history of tuberculosis in any form. There was 1 instance of pulmonary tuberculosis. In another case apical tuberculosis developed during treatment.

In the routine roentgen examination of the chest, there were discovered five additional instances of healed tuberculosis.

I therefore proceeded to search for a focus or foci of infection. The plan of approach included complete physical examination and all allied laboratory studies, complete analysis of the blood, roentgen examination of the chest, examination of the teeth, the nose, the throat and the sinuses, including roentgen studies, and examination of biopsy specimens.

If foci of major importance were found, they were eradicated prior to treatment; with minor foci treatment was instituted coincident with their removal.

There were 8 cases in which both the teeth and the tonsils were involved, and in 3 of these both were removed and the treatment resulted in cure without relapse. In two instances in which neither focus was removed treatment was a complete failure.

Hence, while in a great number of instances the trouble can be laid at the door of infection, it becomes obvious that there must be some other factor or factors at work.

There were 5 instances in which a history of onset after sunburn was definitely established. Of these, the condition was cured in 2 with treatment; in 3 treatment failed. In these 3 there were foci of infection in the teeth. In 2 additional cases there was no history of preceding sunburn, but a recurrence was associated with a definite history of sunburn; in these cases also there were foci of infection in the teeth.

These cases, in the light of the studies done by Drs. Ludy and Corson, are now understandable.

It has been a decided pleasure to have been able to read in detail the data of the authors with regard to the porphyrias and the specific analysis of biopsy specimens, a work which lends the weight of laboratory evidence to a surmise reached by my associates and me from a clinical point of view.

DR. S. W. BECKER, Chicago: I was much interested in the increase of lupus erythematosus in Philadelphia, the report of which gives the members an opportunity to correlate the findings of others with their own.

Several years ago, the late Professor Bloch called my attention to the fact that in his clinic, where he treated ditch diggers and peasants, he observed much lupus vulgaris but little lupus erythematosus; in his private practice there was

much lupus erythematosus but practically no lupus vulgaris—which suggests that lupus erythematosus is a disease of the upper classes, the classes in which the allergic diseases are found.

This assumption would be in line with the increase in lupus erythematosus, since it is known that the neurodermatoses are on the increase owing to the stress and strain of the depression and the increased tempo of modern life.

On the basis of this idea, my associates and I have made it a point to place patients with lupus erythematosus on a modified rest cure, consisting of a daily nap and limitation of activities. Of course, no sunshine is allowed. For patients who have received gold compounds in large amounts after the disease has reached a certain point and refuses to improve further, this regimen of rest has resulted in complete recovery.

DR. THEODORE CORNBLEET, Chicago: I am sure that all dermatologists have at times speculated on the changing character and incidence of various disease entities. In the infectious diseases the immunologic response of the population varies from time to time. In noninfectious diseases undoubtedly the environment has a great deal of influence.

Recently the influence of the weather has come in for a great deal of study in this regard, and I am sure that other elements in the environment will be found to play rôles. In this environment, undoubtedly, the increased use and exposure to metals will undoubtedly be found potent, at least in some persons.

The essayists have posed here the question of the influence of metals externally and their introduction internally in the cause and cure of lupus erythematosus. My interest in this question attaches to a study of one of the lighter metals and its relation to cutaneous disease. Briefly, I have made observations on the excretory activity of the skin in regard to trivalent arsenic and have found that the metal is excreted by the epidermis. In the normal person there is a certain rate at which this arsenic is excreted. However, in 3 persons with arsenical keratoses it was found that there was a retention of metal for an appreciable time.

If I understand the trend in dermatologic research, I expect the relation of metals to cutaneous disease to receive much attention. Even now there is distinct evidence of research in that direction by spectroscopy and the newer microchemical methods.

I am sure that time will show that metals have a profound effect in the production and in the modification of some cutaneous diseases.

DR. M. E. OBERMAYER, Chicago: I was much interested in what Dr. Corson said about the finding of porphyrins in the urine of patients with lupus erythematosus. The prevailing dermatologic conception that porphyrins are found only or mainly in hydroa is not correct, and I feel certain that if systematic investigations were carried out, many more conditions would be found in which porphyria is present.

Only recently Dr. W. J. Turner and I finished a study of porphyria in a case of epidermolysis bullosa, which will be published in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. If such studies were carried out as a routine some light would be shed on a condition of which next to nothing is known.

I should like to ask Dr. Corson what type of porphyrin he found. It is not likely that hematoporphyrin was found, because it is known that hematoporyhyrin is never excreted by human beings.

DR. PAUL E. BECHET, New York: The increased incidence of lupus erythematosus is not confined to Philadelphia. It is marked in New York, and I have

noticed that it is seasonal, the increase being much more notable from August to November than in the winter. I know that in private practice most patients with acute lupus erythematosus of either the discoid or the disseminate type come to me in the late summer or the early autumn. Many of these patients state that the disease apparently began after the subsidence of a severe blistering sunburn. I have long been convinced that actinic exposure is a factor in the production of lupus erythematosus, and its present increased incidence may well be accounted for by the present tremendous popularity of excessive exposure of the skin to the sun or to ultraviolet radiation. I have observed two patients who suffered from acute lupus erythematosus after serious burns from overexposure to ultraviolet ray lamps in their own homes. This entire subject was reviewed by me in a paper read before this section four years ago (ARCH. DERMAT. & SYPH. **29**:221 [Feb.] 1934). The question of heavy metals in lupus erythematosus is extremely interesting. Unfortunately—and this is not in criticism of Dr. Corson's paper at all—one of the faults of a good many of our reports is the fact that controls are not used. The same thing was true some years ago of the reports on the arsenical eczemas. It would be of great value to ascertain if the heavy metals are present in excess or are absent in persons who are free from lupus erythematosus.

DR. RICHARD S. WEISS, St. Louis: I have been interested in lupus erythematosus for many years and have worked with Dr. Mook and others in its study. So far no hint as to the real etiology has been discovered.

I am much interested in the finding of an increase in porphyrin in the urine, but I am wondering whether or not this has any etiologic bearing. It occurs to me that it may be an effect rather than a cause of the disease.

All dermatologists know that in some cases of disseminated lupus erythematosus great damage is done to various organs of the body. That is illustrated frequently at autopsy, and the result of damage to the liver may be porphyrinuria; it certainly seems possible that in these cases the excess of porphyrin is due to hepatic damage. I wonder if Dr. Ludy can give any information on this point.

DR. JOHN B. LUDY, Philadelphia: In a recent Russian publication by W. S. Zhitkova interesting observations are reported in connection with the presence of dust in the atmosphere of factories. The dust of factories contains such metals as lead, iron, copper and chromium in great or small quantities. In some factories the dust scraped from machines contains as much as 8 per cent of lead.

The American National Safety Council established the limit of lead concentration as not higher than 0.6 mg. per cubic meter of air in the dust of factories.

Chronic lead poisoning results from the daily inhalation of as little as 1 mg. of lead per cubic meter of air contaminated with dust.

Chromium is likewise present in the dust of textile mills, leather factories, etc. Definite symptoms result from chronic chromium poisoning, common among which are the so-called "chromium sores" seen on the skin, erosion of the mucous membranes, loss of the nasal septum and chronic bronchitis. Roentgenograms of the lungs of persons suffering from chronic chromium poisoning reveal pictures similar to those of the lungs of subjects with lupus erythematosus.

It is therefore obvious that workers in American factories are in a unique position for reaping the evils resulting from the inhalation of air laden with toxic metals. It is unquestionably problematic just how much air laden with dust containing toxic metals can be inhaled with safety. This of course is dependent on the physical condition of each worker.

The presence of porphyrin in large quantities is an indication of probable hepatic damage and should contraindicate treatment with bismuth or gold compounds for lupus erythematosus.

This question may be naturally asked: What is the relation between lead, chromium or any other metal and lupus erythematosus? It is our opinion, based on recent clinical experience, that these toxic metals act as catalysts. The factors necessary for the production of lupus erythematosus may be (*a*) a focus of infection which affords the necessary antigen, (*b*) a toxic metal, such as lead, which acts as a catalyst and (*c*) sunlight, which affords the ultraviolet rays and thus acts as a spark to the bomb.

Dr. Edward F. Corson, Philadelphia: Dr. Ludy failed to answer Dr. Bechet's question in regard to controls. Forty-one subjects were studied by the method mentioned. Eighteen of these were patients with lupus erythematosus, and 23 were controls. Among the latter group were 3 each with clinical lead poisoning and vitiligo. Cases of the last-mentioned disease furnished the only 3 instances in which lead was found in the skin of the controls.

LUPUS ERYTHEMATOSUS OF THE CONJUNCTIVA

DOUGLASS W. MONTGOMERY, M.D.
SAN FRANCISCO

Lupus erythematosus of the conjunctiva is rare, much less frequently encountered than lupus erythematosus of the mucosa of the lips or mouth.[1] However, when the disease occurs it is important because of its irritability and its obstinacy to treatment, and it may, through atrophy and scarring, cause blindness.[2]

REPORT OF A CASE

A frail woman aged 33 was referred to me by an oculist. She had small erythematous patches scattered over the forehead, nose and cutaneous surface of the upper lip and an unusually irritable refractory conjunctivitis. The condition had been present for more than six months. Two of the lesions on the nose were circular, and each of them had a minute scale on its center. The two lesions on the upper lip were interesting because of their position. They were two faint red spots, one on the lower end of each of the rolls that bound the philtrum. The mucous membrane of the lips was not affected. All of the lesions were smooth with the exception of the minute scales just mentioned.

Having arrived at no definite diagnosis, I was on the point of ordering the use of calamine lotion when the patient remarked that the patches were sensitive to sunlight and had appeared after a severe sunburn. I then found that the patches were sensitive to scratching. It is a curious and interesting feature of lupus erythematosus that, although the patches are neither spontaneously painful nor sensitive to pressure, superficial scratching causes decided discomfort and, more frequently, pain. This pain constitutes an important symptom, especially in cases like the present one, in which hyperkeratosis and implication of the sebaceous glands are either absent or slight.[3]

A rapid summation of the symptoms (erythematous patches down the middle of the face, present for months although very mobile, a tendency to circularity,

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1. Trautmann found in the literature only thirty cases of lupus erythematosus of the mucous membrane of the vermilion border of the lips and mouth. Involvement of the conjunctiva is less frequent (Kren, Otto: Ueber Lupus erythematodes des Lippenrots und der Mundschleimhaut, Arch. f. Dermat. u. Syph. **83**:31, 1907). Only the edge of the lids may be affected (Veiel, F.: Lupus erythematodes, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 2, p. 703).

2. Zinsser: Lupus erythematodes der Bindehaut, Zentralbl. f. Haut- u. Geschlechtskr. **23**:34, 1927. The report deals with lupus erythematosus as causing loss of the eye through cicatricial contraction.

3. In erysipelas, on the contrary, the patch is painful, especially to the touch, and this tenderness to pressure is important for the diagnosis (Milian, G.: Streptocoocides érythémateuses, in Darier, J.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 4, p. 63).

sensitiveness to sunlight and tenderness on superficial scratching) permitted a diagnosis of lupus erythematosus. It was natural to surmise that the obstinate conjunctivitis was the same disease, although it was of an even red color and showed no disks like those that the disease sometimes manifests when it appears on the mucous membrane.

Treatment with sodium gold thiosulfate was instituted all the more willingly as this heavy metal has a special action on the capillaries, and the condition was clearly a capillary disease.[4]

After being under treatment for over a month, the patient told me that as a child of 10 years of age, twenty-three years previously, she had been under my treatment for typical lupus erythematosus with implication of the sebaceous glands. On close inspection, a scar from this previous attack could be seen on the anterior aspect of the left cheek. The scar was superficial, pliable and pitted, as such scars are. After leaving me the patient had been treated for enlargement of the cervical lymphatic nodules, and there still remained many small nodules of both posterior cervical chains and one nodule of the left anterior chain.[5]

The occurrence of lupus erythematosus at such an early age is a rare event, but the details of its appearance and course and the presence of the resultant scar left no doubt as to the correctness of the diagnosis. Recurrent lupus erythematosus is also infrequent, but I regarded its former presence in this case as confirmatory of the nature of the present attack.

Although the red flecks on the upper lip were faint, they were especially tender. As has been mentioned, the flecks were circular dots and were situated exactly bilaterally, one over the lower end of each of the cushions that bound the philtrum. This portion of the lip forms the central segment of the cupid bow mouth of the infant and of the adolescent and the snout of the person of more advanced years. As the snout is a tactile organ, this may account for the unusual sensitiveness of the spots in this situation.

Under treatment with the gold preparation, the conjunctivitis was the first symptom to be favorably affected. The other symptoms lingered, the spots on the upper lip being the last to disappear.

COMMENT

The patient had an irritable conjunctivitis, obstinate to local treatment and associated with flecks of erythema scattered down the middle of the face which were sensitive to sunlight and extremely sensitive to scratching. These flecks were continually present, but, contrary to the usual behavior of lupus erythematosus, they faded and flared rapidly. However, they did not change their site, as the same lesions always

4. Gold does not act on the lupus erythematosus specifically. The action, according to Heubner and Koizumi, is a capillary effect. Gold is a capillary poison whether given as a simple double salt or as an organic compound (Preutz, A.: Die Pharmakologie der Haut: Gold, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, p. 191. Alden, H. S., and Jones, Jack W.: Lupus Erythematosus, J. A. M. A. **107**:1203 [Oct. 10] 1936).

5. Lupus erythematosus has repeatedly been observed to develop with "scrofulous lesions" (Darier, J.: A Textbook of Dermatology, translated by S. Pollitzer, Philadelphia, Lea & Febiger, 1920, p. 573).

flared. They occurred in a frail woman in whom one might suspect tuberculosis, whom I had treated previously for well marked lupus erythematosus and who had suffered from cervical adenitis. Finally, there was the therapeutic effect of gold, known to act favorably, but not specifically, on lupus erythematosus.

Desaux and Boutelier's description of this type of lupus erythematosus is terse and complete.[6] The disease is rare, and desquamation is absent or excessively light. The inflammation is purely congestive. The lesions are mobile but persistent, lighting up and receding rapidly; they do not cause any cicatrix.[6]

The case under discussion is an example of mild diffuse erythematous lupus, and in this variety, according to Kren, the lesions on the mucous membranes are less characteristic of the disease than they are in the discoid variety.[7]

This volatile erythema with its tendency to circularity and lack of scarring is an important type in the philosophy of medicine. For if, as some think, lupus erythematosus and erythema multiforme represent different phases of one disease, this type is the connecting link between the two.

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6. Desaux, A.; Boutelier, A., and Brocq, P.: Manuel pratique de dermatologie, Paris, Masson & Cie, 1932, p. 635.

7. Kren, O.: Mundschleimhautaffektionen: Erythematodes, in Arzt, L., and Zieler, K.: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenburg, 1935, vol. 3, p. 955.

SCLEREDEMA ADULTORUM (BUSCHKE)

S. E. SWEITZER, M.D.
AND
CARL W. LAYMON, M.D.
MINNEAPOLIS

In May 1900 Buschke [1] presented to the Berlin Dermatological Society a man aged 44 in whom a peculiar hardness of the skin had developed after an attack of influenza. The process began on the neck and spread rapidly upward to the face and down the chest and back. Buschke suspected that it was acute scleroderma, but he noted that the involvement seemed much deeper than the usual scleroderma. In the discussion of the case various opinions were expressed: Senator suggested a diagnosis of myxedema; Lesser was reminded of a process similar to sclerema neonatorum, which, however, had not been observed in adults; Blaschko stated that he had seen two patients with the identical condition, which appeared in one patient after scarlet fever and in the other after exposure to cold. Buschke [2] presented a second example of the disease to the same society in 1901, and first formally discussed the condition under the title of scleredema in 1902,[3] when he concluded that it depended on an infiltration deep in the subcutaneous tissues and perhaps in the muscles and was brought about by a disturbance of the lymphatic vessels following an acute infection. Although due credit should be given to Buschke for calling attention to scleredema adultorum, it is likely that the disease had been observed much earlier. Touraine, Golé and Soulignac [4] recently collected reports of ten cases from as early as 1752 to 1865 which were apparently characteristic examples of

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From the Division of Dermatology, University of Minnesota, Dr. H. E. Michelson, Director, and the Dermatology Service, the Minneapolis General Hospital, Dr. S. E. Sweitzer, Chief.

1. Buschke, A.: Presentation of a Case, Arch. f. Dermat. u. Syph. **53**:383, 1900.

2. Buschke, A.: Presentation of a Case, Arch. f. Dermat. u. Syph. **58**:286, 1901.

3. Buschke, A.: Ueber Scleroedem, Berl. klin. Wchnschr. **39**:955, 1902.

4. Touraine, A.; Golé, L., and Soulignac: Sur l'historique du "scléroedème de l'adulte" dit de Buschke, Bull. Soc. franç. de dermat. et syph. **43**:1842, 1936.

scleredema adultorum. The same observers in association with Rabut [5] stated, however, that the disease was not well known among French dermatologists. Although the recent editions of Ormsby's [6] and Sutton's [7] texts contain excellent summaries of available information on scleredema adultorum, the only article in an American periodical is that of Epstein,[8] who in 1932 reviewed forty-one cases in the literature and reported two additional cases. This would indicate that, even though scleredema adultorum may be recognized among dermatologists, scant attention has been given it, and additional observations should be of value. Most of the contributions on the subject have been in German, among which were those of Rissom,[9] Nobl,[10] Bamberger,[11] Roscher,[12] Buschke,[13] Erich Hoffmann,[14] Buschke and Ollendorff,[15] Edmund Hoffmann,[16] Sellei,[17] Freund,[18] Maschkilleisson and Abramowitsch [19] and Ehrmann

5. Touraine, A.; Rabut, R.; Golé, L., and Soulignac: Scléroedème de l'adulte (maladie de Buschke), Bull. Soc. franç. de dermat. et syph. **43**:1634, 1936.

6. Ormsby, Oliver S.: Diseases of the Skin, ed. 4, Philadelphia, Lea & Febiger, 1934, p. 546.

7. Sutton, Richard L.: Diseases of the Skin, ed. 9, St. Louis, C. V. Mosby Company, 1935, p. 590.

8. Epstein, Norman N.: Scleredema Adultorum (Buschke), J. A. M. A. **99**:820 (Sept. 3) 1932.

9. Rissom: Beitrag zur Kenntnis does Sclerödems der Erwachsenen, Arch. f. Dermat. u. Syph. **94**:39, 1909.

10. Nobl, G.: Ueber das benigne Sklerödem der Erwachsenen, Wien. med. Wchnschr. **59**:2244, 1909.

11. Bamberger, E.: Das Sklerödem und seine Beziehungen zu den Sklerodermien, abstr., Arch. f. Dermat. u. Syph. **108**:313, 1911.

12. Roscher: Beitrag zur Kenntnis des Sklerödems Erwachsenen, Arch. f. Dermat. u. Syph. **113**:875, 1912.

13. Buschke, A.: Ueber das Sklerödem und seine Beziehung zur Sklerodermie, Dermat. Wchnschr. **70**:17, 1920.

14. Hoffmann, Erich: Ueber Skleroedema (Skleremia) adultorum nach Grippe mit Veränderungen an den cutanen Nerven, Klin. Wchnschr. **2**:963, 1923.

15. Buschke, A., and Ollendorff, Helene: Skleroedema adultorum mit muskulärer Localisation, Med. Klin. **23**:392, 1927.

16. Hoffmann, Edmund: Das Krankheitsbild des Skleroedema (Skleremia) adultorum (Buschke), Med. Klin. **23**:392, 1927.

17. Sellei, Josef: Skleroedema adultorum (Buschke). (Induratio progressiva benigna sub cute), Dermat. Ztschr. **54**:161, 1928; The Diagnosis and Treatment of Scleroderma and Acrosclerosis and Some of Their Kindred Diseases, Brit. J. Dermat. **46**:523, 1934.

18. Freund, H.: Ueber Sklerödem (Buschke), Arch. f. Dermat. u. Syph. **161**:92, 1930.

19. Maschkilleisson, L. N., and Abramowitsch, L. A.: Scleredema Adultorum Buschke, Dermat. Ztschr. **72**:283, 1935.

and Brünauer.[20] Cases of scleredema adultorum have been presented before various societies by Nobl,[21] Adler,[22] Buschke,[23] Erich Hoffmann,[24] Kumer,[25] Mayr [26] and Freund.[27]

CLINICAL FEATURES

Scleredema adultorum typically is characterized by induration involving the deep layers of the cutis, the subcutaneous tissues, the fascia and the muscles. The condition appears shortly after an acute infectious process, such as grip, influenza, scarlet fever, measles, mumps or angina. It usually begins on the nape of the neck and spreads rapidly by continuity to the face, the shoulders, the arms, the back, the chest and the abdomen. In contrast to diffuse scleroderma, the hands and the feet are not affected. Although the cutaneous hardness is painless, the involved areas feel tense, and interference with mobility is not uncommon. Chewing, talking and the movements of respiration become difficult. The patient frequently states that he feels as though he were enclosed in a suit of armor. The smaller folds of the skin are lost, and when palpated the tissues feel as if they were permeated by paraffin. The induration is deep and extremely firm, and pitting like that associated with ordinary edema it is impossible to elicit. Important disturbances of sensation or sweating are not usually present. The skin is generally cool and pale, although erythematous patches or a livid hue has been noted.

The disease reaches its height within a few weeks, after which there is a stationary period of variable length. In practically all cases there is complete involution within eighteen months. Females are more frequently affected than males. Of sixteen patients whose cases were reviewed by Edmund Hoffmann, only five were males. The disease has occurred at various ages from infancy to middle adult life. Cases of

20. Ehrmann, S., and Brünauer, R.: Sclerodermie, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 717.

21. Nobl, G.: Presentation of a Case, Arch. f. Dermat. u. Syph. **107**:440, 1911.

22. Adler: Sklerödem vor 30 Jahren, Zentralbl. f. Haut- u. Geschlechtskr. **20**:259, 1926.

23. Buschke, A.: Muskuläre Lokalisation des Scleroedema adultorum, Zentralbl. f. Haut- u. Geschlechtskr. **25**:513, 1928.

24. Hoffmann, Erich: Scleroedema adultorum (Scleremia), Arch. f. Dermat. u. Syph. **115**:319, 1928.

25. Kumer: Sklerödem der Erwachsenen (Buschke), Wien. klin. Wchnschr. **42**:1369, 1929.

26. Mayr, J.: Das Krankheitsbild des Scleroedema adultorum Buschke, Zentralbl. f. Haut- u. Geschlechtskr. **31**:428, 1929.

27. Freund, H.: Histologische Befunde bei Sklerödem (Buschke), Zentralbl. f. Haut- u. Geschlechtskr. **33**:303, 1930.

so-called scleroderma in infants have been thought by some observers to be instances of scleredema.

Recurrences of the condition after apparent recovery have been reported by Adler, Bamberger and Epstein. Adler's patient had the first attack at the age of 26, after scarlet fever, and complete recovery followed; the second attack occurred at the age of 35. Bamberger's patient had scleredema at the ages of 20 and 26, in each instance after influenza; there was complete disappearance of the induration between the attacks. Each of Epstein's two patients had two attacks, the first patient at the ages of 15 and 31 and the second patient at the ages of 16 and 43. An acute febrile process preceded each attack.

Like any other disease, scleredema adultorum is subject to variations from its usual form. It may begin in an area other than the neck, such as the back or the buttocks. In all cases, however, it spreads by continuity and leaves the hands and feet free. Its course, moreover, may be extremely prolonged. Adler's patient still has a residual swelling of both eyelids thirty years after the disease appeared.

HISTOLOGIC STRUCTURE

The essential pathologic alterations in scleredema adultorum appear chiefly in the deeper portions of the cutis, any superficial changes being secondary. In a detailed histologic study of the disease, Freund found that there was an edematous loosening of the collagen bundles by a metachromatic, mucin-like substance, which he believed caused the palpable induration. As a result of the permeation of this peculiar substance, there were swelling of the connective tissue fibers and vacuolation in the cutis. These changes existed in conjunction with a nonspecific cellular infiltrate about dilated blood vessels and an increase in fibroblasts, resulting in the formation of new connective tissue. This unknown substance, which stained best with cresyl violet, was thought by Freund not to be true mucin. Buschke and Ollendorff likewise noted an amorphous substance, which even penetrated the muscles, in a case in which there was deep involvement. Necrosis of the tissues was absent.

The elastic fibers are in general normal, although they may appear to be short, split or torn by the exudative process. Erich Hoffmann demonstrated changes in the cutaneous nerves in scleredema adultorum. The affected nerves were thickened, swollen and surrounded by a round cell infiltrate. The vasa nervorum were dilated.

ETIOLOGY

Although the cause of scleredema adultorum is not definitely known, its occurrence shortly after various acute infections suggests that it is intimately related to toxins which cause an exudation of a mucin-like

substance into the tissues. Erich Hoffmann's findings suggested that these toxins affected the cutaneous nerves, thus altering the nutrition of the cutaneous connective tissue. Buschke first expressed the belief that a lymph stasis explained the clinical findings, and Rissom later expressed concurrence in this opinion.

By means of the atoxyl lipase resistance test Sellei found a disturbance in the enzymes in two cases of scleredema.

Various observers have suggested a disturbance in the endocrine system as an etiologic factor. In one of Freund's cases a tumor in the hypophysial region and destruction of the sella turcica were demonstrated by roentgenograms. In the same case the thyroid was enlarged and firm, although treatment with solution of posterior pituitary and with thyroid apparently had no appreciable influence on the course of the disease. In most cases of scleredema adultorum the induration in the neck is so intense that it is impossible to determine whether or not the thyroid is of normal size. Both hyperfunction and hypofunction of the thyroid have been observed in cases of scleredema by various observers, but there has been no constant relation to either.

Other glands, such as the ovary and the thymus, have been suspected of bearing some causative relation to scleredema in isolated cases, but as yet it is impossible to form a conclusive opinion.

DIAGNOSIS

The first step in the diagnosis of scleredema adultorum is its differentiation from diffuse scleroderma, especially during the acute stages of both diseases. The facts that scleredema adultorum follows an acute infection, seems deeper in the cutis, lacks the characteristic ivory color of scleroderma and never presents pigmentation or atrophy are the most important aids in diagnosis. Scleroderma lacks any definite relation to infection and usually begins on the hands or the feet, while scleredema never involves those portions of the body. A period of observation may be necessary to establish the diagnosis as scleredema follows a more rapid course and as a rule regresses spontaneously, while diffuse scleroderma is slowly progressive.

In the rare instances in which scleredema (Buschke) occurs in infants, it must be distinguished from sclerema neonatorum (sclerema adiposum), œdema neonatorum (sclerema œdematosum) and subcutaneous fat necrosis. All three diseases are uncommon and appear soon after birth. These diseases were recently discussed in a masterly manner by Fox.[28]

28. Fox, Howard: Subcutaneous Fat Necrosis of the New-Born, Arch. Dermat. & Syph. **27**:237 (Feb.) 1933.

Sclerema neonatorum occurs in weak, debilitated infants and is frequently accompanied by severe diarrhea and dehydration. The affected infant actually seems to shrink. The skin feels cold and is white or yellowish white. The body temperature is usually subnormal, and in most instances death occurs within a few days. The condition begins on the lower extremities and spreads rapidly upward, in contrast to scleredema, which usually begins in the region of the neck.

Œdema neonatorum occurs in weak or premature infants. In this disease the skin appears swollen and edematous, rather than shrunken as in sclerema neonatorum. The affected parts (the extremities, the mons veneris and the eyelids) may be red at first and change to yellowish later in some cases. In œdema neonatorum the body temperature is usually low and the outcome lethal, affording a sharp contrast to scleredema, in which the general health is unaffected.

Subcutaneous fat necrosis of the newborn, thought to be due to trauma following prolonged or difficult labor, does not present a serious problem in differentiation from scleredema. The lesions in subcutaneous fat necrosis consist of fairly well circumscribed hard nodules, usually located on the back or the buttocks, in contrast to the diffuse involvement in scleredema. In the former condition the tumefactions are situated in the subcutaneous tissues and appear from two to twenty days after birth. The skin overlying the lesions is usually bluish red. The disease usually ends in complete involution within a few months, and the general health is not affected.

Scleredema adultorum is not likely to be confused with dermatomyositis, since the latter is a febrile disease usually accompanied with pain and tenderness when pressure is applied to the involved muscles. The onset of dermatomyositis is usually insidious and is not constantly associated with an acute infectious disease, as is the case with scleredema. Fever and constitutional symptoms, such as malaise, extreme weakness, fatigue and paresthesia, are common in cases of dermatomyositis and rare in cases of scleredema. Dermatomyositis is frequently accompanied with cutaneous eruption simulating urticaria, erysipelas, erythema multiforme or erythema nodosum, a feature which is absent in cases of scleredema. According to Wheeler and Harbin,[29] who completely reviewed the subject in 1932, the prognosis of dermatomyositis is unfavorable in 50 per cent of the cases, many patients dying in from two or three weeks to three or four months.

Scleredema bears little resemblance to trichinosis. In typical cases the latter disease is characterized by digestive disturbances, muscular tenderness and continuous fever. The tenderness is usually most severe

29. Wheeler, Philip H., and Harbin, Maxwell: Dermatomyositis, Arch. Dermat. & Syph. **26**:1039 (Dec.) 1932.

in the muscles of the extremities, although the muscles of speech, mastication and respiration may be affected. Edema of the face and extremities may be present, but it does not resemble the subacute, deep induration of scleredema. The leukocyte count is usually high, reaching 30,000 in some instances, and there may be as many as 50 per cent eosinophils; these features are lacking in scleredema.

The clinical features of myxedema render differentiation from scleredema relatively easy. The onset of myxedema is usually insidious. There is a gradual slowing of the mental and bodily activities, with decreased appetite, increased weight and a change in facial expression. The skin is dry and scaly, in contrast to its smoothness in scleredema. In myxedema the cutaneous induration is usually most intense on the hands and the feet, while scleredema spares these parts. The basal metabolic rate is uniformly low with myxedema, and variable with scleredema.

THERAPY

Since spontaneous involution generally occurs in scleredema adultorum, it is difficult to evaluate the various therapeutic measures which have been used. Sodium salicylate, thyroid and other glandular extracts have been administered internally, while warm baths, massage and the application of heat (diathermy) have apparently been of some value in causing a regression of the disease. Too favorable a prognosis should not be given, since it is impossible to predict exactly when the condition will subside.

REPORT OF CASES

CASE 1.—*History.*—E. J., a white girl aged 14, of Scandinavian descent, was first seen in Dr. H. E. Michelson's clinic at the University of Minnesota Hospital. During the last part of April 1936 she had an attack of grip with acute angina and pains in the bones and the muscles, which persisted throughout the first part of May. During the last week in May the patient noted that the skin on the back of her neck was becoming stiff and was impairing motion to a certain extent. This condition rapidly spread to the chest and the back but progressed no lower than the waistline. The induration of the skin of the chest made respiration rather difficult. The health of the patient had always been excellent.

Physical Examination.—The patient was well developed and appeared to be in good health. The abnormality of the skin involved the entire neck posteriorly and anteriorly, as well as the chest and the back. The lower half of the body, the face, the hands and the feet were normal. The essential cutaneous changes consisted of abnormal firmness, apparently situated deep in the tissues. There were no surface changes. Neurologic examination showed no disturbance of sensation in the affected areas. The general physical examination showed no important deviations from normal.

Laboratory Examination.—Examination of the urine showed no abnormalities. Examination of the blood showed 77 per cent hemoglobin, 8,400 white cells, 59 per cent polymorphonuclears, 35 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. The nonprotein nitrogen content of the blood was 24.3 mg.

per hundred cubic centimeters. The chloride content of the serum was 351.1 mg. per hundred cubic centimeters; the calcium content, 11.5 mg.; the phosphorus content, 4.6 mg.; the potassium 18.8 mg., and the total protein content, 7.54 mg. (albumin, 4.38 mg., and globulin 3.16 mg.).

The basal metabolic rate, determined on two occasions shortly after admission to the University of Minnesota Hospital, was —30 and —34 per cent.

Course.—The patient was given desiccated thyroid. When she was last seen, in April 1937, approximately a year after the onset of the disease, the eruption had not cleared completely in any of the originally affected parts. She stated that when she was warm the skin was almost as soft as normal but that it would become stiff again for two or three days after exposure to cold. There was definite improvement in all areas, however, none of them being as hard as they had been in the beginning. The response to thyroid was not that which would be expected in a case of myxedema.

Histologic Examination.—An elliptic piece of skin from the shoulder was excised for histologic study. The tissue was fixed in a 10 per cent dilution of solution of formaldehyde, U. S. P., embedded in paraffin, sectioned in the usual manner and stained with hematoxylin and eosin, Unna's polychrome methylene blue solution, gentian violet and Weigert's and Van Gieson's stain.

In the sections stained with hematoxylin and eosin the epidermis and the papillary portion of the cutis appeared normal. The sudoriparous and sebaceous glands were intact and of normal number. The important pathologic changes were seen in the lower two thirds of the cutis and the subcutaneous tissue. In the affected zones the bundles of connective tissue appeared greatly swollen and much thicker than normal and throughout the tissue seemed separated by some substance which was not affected by the stain. There was no striking increase in the number of fibroblasts. Clear unstained spaces of various sizes were much in evidence in the affected parts. Throughout the cutis there were sparse collections of lymphocytes about slightly dilated blood vessels, although the inflammatory features were not outstanding. The subcutaneous fat was present in normal amount and showed no evidences of inflammatory infiltrate, although in several places accumulations of an amorphous, indefinitely outlined light violet substance could be seen.

In the sections stained with the Weigert stain the elastic fibers in the papillary portion of the cutis were normal. In the lower two thirds of the section, however, the elastic fibers seemed pushed apart by the infiltrative process.

The Van Gieson stain showed definite tinctorial changes, the entire cutis being yellowish green instead of the usual red.

Sections stained with gentian violet failed to disclose amyloid.

The tissues stained with Unna's polychrome methylene blue solution showed that the substance in the tissues did not assume the red color characteristic of mucin. The groundwork of the entire cutis was light greenish blue.

In brief, the histologic changes consisted of swelling and separation of the connective tissue fibers of the lower two thirds of the cutis and clear spaces of various sizes.

CASE 2 (Dr. H. E. Michelson).—*History.*—N. H., a white boy aged 16, had scarlet fever during the first week of January 1936. The disease was mild, although he had angina and a characteristic eruption. About February 1 the patient noticed that the skin on the back and the sides of his neck felt tight. In the next few weeks similar changes developed on the shoulders, the arms as far as the elbows, the chest, back and the abdomen. The buttocks, the pubic region,

the forearms, the hands and the lower extremities remained normal. Although the lower jaw could be moved without difficulty, the patient noticed that he was unable to project his tongue to the same extent as he could before the onset of the disease. The cutaneous lesions were not painful, and the general health was good.

Physical Examination.—The patient was well developed and did not appear ill. The neck, the chin, the tongue, the shoulders, the upper portions of the arms, the chest, the back and the abdomen were affected by the pathologic process. The hands, the forehead, the cheeks, the scalp, the buttocks, the genitalia and the lower extremities were normal. The affected areas showed no surface change but felt as if the deeper portions of the skin were filled with putty. There was no pitting when pressure was applied. The neck could be rotated with difficulty, and normal

Scleredema adultorum, showing edematous loosening of the collagen bundles with the formation of spaces in the cutis.

projection of the tongue forward was impossible, although its movement inside the mouth was possible.

Laboratory Examination.—Serologic tests for syphilis were negative. The urine showed no abnormalities. A blood count showed 80 per cent hemoglobin (Sahli), 8,200 white cells, 70 per cent polymorphonuclears, 24 per cent lymphocytes and 2 per cent eosinophils. The sugar content was 110 mg. per hundred cubic centimeters; the cholesterol content, 192.3 mg. The basal metabolic rate was —13 per cent.

Course.—One year after the onset of the disease the patient reported that considerable softening had occurred in all the affected areas, although a complete return to normal had not taken place. Improvement was slow but steady.

Histologic Examination.—The histologic examination showed essentially the same features as were noted in case 1.

COMMENT AND SUMMARY

Scleredema adultorum is a rare disease, if one may judge from the small number of articles on the subject. Despite several plausible theories, its etiology is obscure. The constant association of scleredema with various acute infections suggests that some unknown toxin probably affects the vegetative nervous system and the glands of internal secretion, resulting in the deposit of a mucinous substance in the skin. The exact nature of this material is unknown. Freund, after a thorough histochemical study of the substance, expressed the belief that it was definitely not mucin but probably closely related, belonging in the same group of chemical compounds.

Although the basal metabolic rate of both of our patients was below normal, such a finding is not new and should be regarded as no more than coincidental, since there was no definite response to thyroid. It is doubtful if the course of the disease in either patient was influenced by the medication given.

The diagnosis of scleredema is not difficult. The onset following an acute infection, the rapid progression and the benign course stand in sharp contrast to the features of diffuse scleroderma, with which it is most likely to be confused. The usual localization on the back of the neck at the time of onset and the lack of involvement of the hands and the feet are other points which aid in the differentiation of scleredema adultorum from scleroderma.

The changes seen histologically consist chiefly of swelling and separation of the bundles of connective tissue in the cutis, resulting in the formation of clear spaces of various sizes. Signs of inflammation are slight.

In conclusion it may be said that scleredema adultorum is a definite entity with characteristic clinical features and terminates in complete involution in a majority of cases.

NOTE.—Since this paper was submitted for publication an additional case has been reported.[30]

ABSTRACT OF DISCUSSION

DR. N. N. EPSTEIN, San Francisco: In the two cases which I reported a few years ago recovery was not complete at the time of the report. Between five and six years elapsed after the onset of the condition before these patients were able to resume normal activity. Scleredema adultorum seems to have a striking and similar onset in most cases, starting on the back of the neck and continuing downward to disappear imperceptibly on the lower limbs. The pathologic picture shows why the skin heals without any serious damage. There is little inflammatory reaction. The disease consists simply of an increase in the size of the collagen bundles and the deposit of a mucin-like material in the tissues. There is no endarteritis,

30. Frank, L. J.: Scleredema Adultorum (Buschke), Arch. Dermat. & Syph. **36**:1052 (Nov.) 1937.

and therefore the circulation of the skin is not impaired. In my original paper I expressed the belief that this condition was probably much more common than was believed previously, but a case has not been observed since that time.

DR. PAUL A. O'LEARY, Rochester, Minn.: I cannot agree with Dr. Sweitzer that the differentiation between scleredema adultorum and scleroderma is as simple as he pictures it. I believe that a dermatologic neophyte should recognize scleroderma after it has been present for a year or two, but in the early stages of the two diseases I find it difficult to distinguish between them.

I do agree with Dr. Sweitzer that scleredema runs a limited course and as a rule involutes spontaneously. This is not true, however, of scleroderma. Hence, there is a need for an accurate differentiation if a prognosis is to be given.

The clinical picture of dermatomyositis, shortly after its onset, is similar to that of scleredema and that of scleroderma when the head, the upper part of the trunk and the arms are the areas first involved. This adds further to the difficulties of differential diagnosis. For several years I have been examining specimens of muscle from patients with dermatomyositis, scleredema and scleroderma, in the belief that it would help materially in arriving at an accurate diagnosis shortly after the onset of symptoms. Thus far I have found that the changes in the muscles are not of diagnostic value, although in cases in which scleroderma or dermatomyositis is of long standing the muscles present characteristic changes.

Further, I believe that scleroderma is a syndrome of which there are not only various types but various causes, so that it is necessary to state the type of scleroderma when discussing it. Acrosclerosis of Sellei is merely one form of the disease with a characteristic distribution.

I do agree with Dr. Sweitzer that scleredema is self limited, and it is accordingly unnecessary to use radical therapeutic measures in its treatment.

DR. S. E. SWEITZER, Minneapolis: I said not that scleroderma does not appear on the hands but that scleredema adultorum does not appear on the hands.

The diagnosis is not as difficult as Dr. O'Leary says, as he successfully diagnosed the condition in eight cases of his own. Caution must be exercised when a case is first observed, as early scleroderma may resemble scleredema. The history of the disease following a previous illness helps materially in the diagnosis.

SEROLOGIC EVIDENCE OF SYPHILIS IN MALARIAL PATIENTS

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In June 1935 the committee on evaluation of serodiagnostic tests for syphilis first reported [1] on the frequency of positive reactions among patients with malaria. It will be recalled that the tests were performed by thirteen of the foremost serologists in America. A total of 457 tests of specimens from 36 malarial donors were studied, and there were 66, or 14.4 per cent, positive reactions and 6.1 per cent doubtful reactions. For only 14 of the 36 patients was there complete accord among the results obtained by the serologists. In tests that were repeated the results but rarely tallied with the original ones, some of the original reports being negative while repeated determinations were positive.

A second study recently completed included a total of 266 patients, with 4 tests made in most cases, for a total of 1,031 comparable tests. The tests were done by Hinton, Kline (using both diagnostic and exclusion tests) and Kolmer. The 266 donors were white persons from South Carolina and Georgia. History and physical examination gave no indication of syphilis.

Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 5, 1937.

1. Cumming, H. S.; Hazen, H. H.; Sanford, A. H.; Senear, F. E.; Simpson, W. M., and Vonderlehr, R. A.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States, J. A. M. A. **104**:2083 (June 8) 1935; Ven. Dis. Inform. **16**:189, 1935.

OCCURRENCE OF POSITIVE RESULTS

The results of the serologic examinations are shown in table 1. It will be noted that the percentage of positive reports is not so high as it was in the first study but is higher than that to be expected among white subjects when care has been taken to exclude syphilis.

DEGREE OF AGREEMENT OR DISAGREEMENT

The agreement or disagreement among serologists is shown in table 2. It will be noted that for 191 patients, 71.8 per cent, all

TABLE 1.—*Results of Serologic Tests for Syphilis of Specimens of Blood from 266 Presumably Nonsyphilitic Patients with Malaria*

Examiner	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged
Hinton	250	12	11	4.4	16
Kline (diagnostic test)	259	17	16	6.2	7
Kline (exclusion test)	259	22	42	16.2	7
Kolmer	263	0	13	4.9	3
Total	1,031	51	82	8.0	33

TABLE 2.—*The Number of Specimens of Blood in a Group of 266 Presumably Nonsyphilitic Patients with Malaria on Which There was Complete Agreement Among the Examiners and the Number on Which There was Disagreement*

Degree of Agreement or Disagreement Among Examiners	Specimens of Blood	
	Number	Percentage
Number on which all agreed:		
Negative findings	191	71.8
Positive findings	6	2.3
	197	74.1
Number on which there was some disagreement:		
Number on which 1 disagreed	36	13.5
Number on which 2 disagreed	26	9.8
Number on which 3 disagreed	7	2.6
	69	25.9
Total	266	100.0

examiners recorded negative findings and that in 6 instances, 2.3 per cent, all reported positive findings. For 69 patients, 25.9 per cent, the results disagreed. Much the highest percentage of both positive and doubtful reports was given by the Kline exclusion test and the lowest percentage of positive reports by Hinton's method. Kolmer reported no doubtful results. The amount of disagreement reminds one of the reports of the committee on leprosy.[2]

2. Hazen, H. H.; Parran, Thomas; Sanford, A. H.; Senear, F. E.; Simpson, W. M., and Vonderlehr, R. A.: The Occurrence in Leprosy of Positive Serodiagnostic Tests for Syphilis, Ven. Dis. Inform. **17**:253, 1936; Internat. J. Leprosy **4**:315, 1936.

EXCLUSION OF SYPHILIS

In the study here reported there were 82 positive and 51 doubtful reports. Rechecks were not included in these figures. Serologic examinations were repeated on 49 of the 51 donors who showed one or more positive reactions, with the result that there was a decrease of 24 in a total of 80 positive reports. It is worthy of note that among 68 specimens from 18 white girls less than 10 years of age there were 13.2 per cent that were positive, the highest percentage in any age group except that from 60 to 69 years. Female subjects showed a higher percentage of positive results than did males. Such figures do not follow the usual trend of the prevalence of syphilis (table 3). The results according to age are shown in table 4. There is a striking dissimilarity of positive

TABLE 3.—*Results of Serologic Tests for Syphilis on Specimens of Blood from 161 White Males and 105 White Females With Malaria and Presumably Without Syphilis*

	White Males					White Females				
Examiner	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged
Hinton.....	153	8	5	3.3	8	97	4	6	6.2	8
Kline (diagnostic test).....	157	12	8	5.1	4	102	5	8	7.8	3
Kline (exclusion test).....	157	12	23	14.6	4	102	10	19	18.6	3
Kolmer.....	159	0	8	5.0	2	104	0	5	4.8	1
Total.....	626	32	44	7.0	18	405	19	38	9.4	15

reports for the different age groups. There were not enough patients over 40, however, to enable the safe drawing of any deductions. The difference between results for patients in the various decades of life is striking.

RECHECKS

Table 5 shows the results of rechecks on the serum of 49 of 51 subjects who had positive reactions. The number of repeatedly positive reports dropped to 56. The Kline diagnostic test gave the same percentage of positive results in both series.

Fischer and Günsberger [3] stated that patients with malaria may show a positive Wassermann reaction during the attack and for some time afterward. The authors described experiments showing that this

3. Fischer, O., and Günsberger, O. D.: Cause of the Positive Wassermann Reaction in Malaria, Ztschr. f. Immunitätsforsch. u. exper. Therap. **78**:295, 1933.

positive Wassermann reaction in malaria is due to the presence of specific antibodies for erythrocyte lipoids. They described an extract of ox heart which was relatively poor in erythrocyte lipoids and which, although it is a good syphilitic antigen, reacts not at all or only slightly

TABLE 4.—*Results of Serologic Tests for Syphilis on Specimens of Blood from 161 White Males and 105 White Females With Malaria and Presumably Without Syphilis, Classified According to Age*

	White Males					White Females				
Age Group, Years	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged
Less than 10.....	53	1	2	3.8	3	68	1	9	13.2	4
10-19.....	258	15	14	5.4	6	154	9	10	6.5	6
20-29.....	200	7	16	8.0	8	67	3	6	9.0	1
30-39.....	32	2	6	18.8	0	50	2	4	8.0	2
40-49.....	36	1	1	2.8	0	26	1	3	11.5	2
50-59.....	39	5	5	12.8	1	24	1	2	8.3	0
60-69.....	4	1	0	0.0	0	12	2	4	33.3	0
70-79.....	4	0	0	0.0	0	4	0	0	0.0	0
Total.....	626	32	44	7.0	18	405	19	38	9.4	15

TABLE 5.—*Comparison of the Serologic Tests for Syphilis on Specimens of Blood from 49 Presumably Nonsyphilitic Patients on Whom Serologic Rechecks Were Made*

	Original Reports					Rechecks				
Examiner	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged	Total Specimens Examined	Number of Doubtful Reports	Number of Positive Reports	Percentage of Positive Reports	Specimens Hemolyzed or Physically Damaged
Hinton.....	49	6	11	22.4	0	45	6	6	13.3	4
Kline (diagnostic test).....	49	15	16	32.7	0	49	8	16	32.7	0
Kline (exclusion test).....	49	4	40	81.6	0	49	7	29	59.2	0
Kolmer.....	49	0	13	26.5	0	49	1	5	10.2	0
Total.....	196	25	80	40.8	0	192	22	56	29.2	4

in malaria. If the Wassermann test is carried out both with the erythrocyte extract and with Wassermann extracts, Wassermann-positive malaria can be differentiated from syphilis, an accomplishment of value in regions infested with malaria.

Businco and Foltz [4] concluded that strongly positive reactions in either acute or late malaria are due to concurrent syphilis. Of subjects with acute febrile malaria, 11 per cent had a partially positive complement fixation reaction for syphilis, which must be considered nonspecific. The serum was anticomplementary in 8 per cent of the patients with acute malaria.

Cherefeddin [5] reported results of the Wassermann test in 76 cases of malaria. There were 10 positive responses, which is not a high percentage. This investigation was made because it was known that the Wassermann reaction sometimes becomes positive in acute or chronic malaria and because in countries where malaria is prevalent such reactions may be of considerable significance.

Eller [6] examined malarial patients who were free from syphilis by methods usually used for the serologic diagnosis of syphilis. In some cases he obtained positive results which could not be distinguished from those in cases of syphilis. This was true both in spontaneous malaria and in that induced by inoculation. The nature and the constancy of occurrence of the positive Wassermann reaction in certain stages of inoculation malaria suggest that processes must take place in malaria which are similar to those that bring about a positive Wassermann reaction in syphilis. The processes cannot be exactly the same, however, as there are differences in the reaction to the Meinicke turbidity test in the two diseases. Apparently the products of the reaction in the serum of patients with malaria and syphilis differ both quantitatively and qualitatively. In malaria these products are not immune bodies. A further study of this question will be of clinical interest in the differential diagnosis between malaria and syphilis, which is important not only in the tropics but in the temperate zone, because of the therapeutic use of inoculation malaria. It will be of value in explaining the nature of the serologic reactions and particularly in separating the antigen-antibody reactions from reactions of pure lability.

Lloyd and Mitra [7] discussed the literature on the Wassermann reaction in malaria. They used a sensitive system, putting up each serum against three antigens—cholesterolized alcoholic Bordet's, and cholesterolized Bordet's, when estimating the effect of treatment. Of 85

4. Businco, A., and Foltz, P.: Syphilis and Malaria: Value of Biological Examinations, Policlinico (sez. med.) **31**:245, 1924.

5. Cherefeddin, Osman: Wassermann Reaction in Malaria, Arch. f. Schiffs- u. Tropen-Hyg. **34**:282, 1930.

6. Eller, Karl: Serologic Studies of Tertian Inoculation Malaria in Patients Free of Syphilis, Ztschr. f. Immunitätsforsch. u. exper. Therap. **74**:397, 1932.

7. Lloyd, R. B., and Mitra, G. C.: The Wassermann Reaction in Malaria, Indian J. M. Research **14**:135, 1926.

cases of malaria, the results were fully positive in 4, partially positive in 8, negative in 61 and incompletely negative in 12. In only 1 of the 12 cases in which there was a positive reaction was there a definite history of syphilis. Since 14 per cent is well within the rate for syphilis in Calcutta, India, there is no evidence that in the cases of malaria in which there was a positive reaction the reaction was due to malaria.

Lloyd [8] stated that positive reactions in malaria or leprosy are due either to associated syphilis or to oversensitive tests. Every investigator in the tropics must adjust his technic so that malaria in the febrile stages, uncomplicated by syphilis, will yield a negative reaction. It is only in the febrile stage that positive results are obtained. Changes in technic that will exclude malaria are comparatively simple, but for leprosy radical alterations are necessary; it appears that the factor causing false positive reactions is weak in malaria but strong in leprosy.

Marcialis [9] investigated 225 cases, comprising 44 of tertian, 58 of quartan and 71 of subtertian malaria and 52 in which no parasites were found (the condition in 40 of these being classed as chronic malaria and in 12 as malarial cachexia). It transpired that in apyrexial periods no positive Wassermann reaction was produced but that during fever a slight reaction was occasionally detected, irrespective of the presence, the kind or the number of parasites evident in the peripheral blood. The Sachs-Georgi test with the thermostat gave generally corresponding results. Injections of quinine or its admixture with the serum in vitro did not alter the reaction.

Salvioli [10] found that serum from certain persons with acute malaria gives weakly positive Wassermann reactions. He advised that in a malarial region the Sachs-Georgi or the Meinicke test should be substituted for, or at least used in addition to, the Wassermann test as a check on nonspecific reactions produced by the latter.

Saunders and Turner [11] concluded that malaria alone does not cause fixation of the complement in the Wassermann reaction with the methods used, but there is evidence to show that acute malaria may act as a provocative agent to bring a reagin of low titer up to the threshold where fixation of the complement becomes obvious in the tests. Malaria

8. Lloyd, R. B.: The Interpretation of Wassermann Results in India, Indian M. Gaz. **77**:10, 1932.

9. Marcialis, G.: Wassermann and Sachs-Georgi Reactions in Malaria, Gazz. d. osp. **45**:75 (Jan. 27) 1924; Trop. Dis. Bull. **21**:612, 1924.

10. Salvioli, Gaetano: The Seroreactions of Syphilis in Malaria, Gazz. d. osp. **44**:374 (April 22) 1923; Trop. Dis. Bull. **20**:975, 1923.

11. Saunders, George M., and Turner, Thomas B.: The Wassermann Reaction in Malaria, South. M. J. **28**:542, 1935.

may produce anticomplementary reactions, but usually in partly positive serum. They stated:

(1) . . . In a locality [Jamaica] where yaws is endemic patients showing positive Wassermann reactions gave a definite history of yaws in all but about 17 per cent of the cases studied.

(2) The Wassermann reactions in a series of patients with malaria agreed almost exactly with the reactions among the general population of the area.

(3) In 135 malaria patients, 70 of whom had acute febrile manifestations, the Wassermann reaction was negative in all cases.

(4) In 123 malaria patients whose Wassermann reactions were positive or partly positive, yaws or syphilis was the assigned cause of the positive test in all but 15 cases. Thirteen of these showed consistently positive reactions before and after the attack of malaria. Two had only one observation each.

(5) In 8 yaws patients who had had positive Wassermann reactions reverting to negative after specific therapy, the Wassermann reaction remained negative during subsequent attacks of acute malaria.

(6) In two patients, both of whom had had yaws but whose Wassermann reactions had become negative, there was slight fixation of the complement with 0.1 cc. of serum in each case during an attack of malaria.

(7) Most of the patients with anticomplementary reactions had had yaws. The percentage of anticomplementary reactions was higher for the malaria patients than for the general population.

Wilson and Levin [12] investigated the records of 262 cases of malaria at the Roper Hospital, Charleston, S. C., for evidence that might aid in determining whether falsely positive reactions to tests for syphilis may be obtained in malaria. Throughout the study, from 1930 to 1934, the Kolmer test was used; in addition, during 1930 and 1931 the standard Kahn test was used as a routine, while from 1932 to 1934 the Kline diagnostic test was used. Positive reactions were obtained in 70 cases. In interpreting these positive findings the authors studied all relevant data that could be obtained, such as a suggestive history of primary or secondary lesions of syphilis, a history of previous syphilitic treatment, the results of previous and subsequent serologic tests, physical findings suggestive of syphilis and findings compatible with that diagnosis and for which another diagnosis was not found. On these criteria they based the belief that in 13 cases the positive reaction was definitely due to malaria and in 2 it was possibly so. The tests used in these 13 cases were those of Kolmer and Kline. Of the 13 cases there was agreement between the tests in 5 and complete disagreement in 8; of the latter the Kline test remained negative in 6 and the Kolmer test in 2.

Heinemann [13] examined laborers, both male and female, in Java. A special feature of syphilis in that country is that neither tabes dorsalis

12. Wilson, Robert, Jr., and Levin, Stanley L.: Observations on the Effect of Malaria on the Wassermann Reaction, Am. J. M. Sc. **191**:696, 1936.

13. Heinemann, H.: Studies on Cerebrospinal Fluid, Arch. f. Schiffs- u. Tropen-Hyg. **28**:26, 1924; Ven. Dis. Inform. **5**:245, 1924.

nor progressive paralysis is known. Malaria has often caused errors in the serologic diagnosis of the blood, and it was interesting, therefore, to ascertain whether that would be true of the cerebrospinal fluid. The fluids of 150 patients with malaria were studied. The author found that malaria caused no errors in examination of the spinal fluid with the Wassermann and the Meinicke test.

Wise and Sulzberger [14] in commenting on a paper on the occurrence in leprosy of positive serologic evidence of syphilis by the committee for evaluation of serodiagnostic tests for syphilis stated:

> By the dissociation method of Witebsky the true immunologic positive complement fixation of syphilis may be distinguished from the pseudopositives probably due to nonimmunologic disturbances of colloid dispersion.

A number of suggestions have been made for the modification of serodiagnostic methods so that they will give positive results in syphilis but not in malaria or leprosy. Whether or not these modifications are sufficiently simple for any well equipped laboratory to effect is still a debatable question. It is probable that studies as to the fundamental nature of serodiagnostic tests for syphilis are necessary before it is really profitable to discuss many such suggestions.

COMMENT

It seems safe to assume that malaria, like leprosy, can be the cause of positive serologic reactions to tests for syphilis. It is probable that more than one patient has been placed under treatment for syphilis when malaria was the cause of his positive serologic reaction. It seems odd that positive reactions are due to diseases caused by such biologically different organisms as an acid-fast bacillus, a spirochete and a plasmodium. It may be necessary to investigate anew the causation of certain of these diseases, notably that of leprosy.

ABSTRACT OF DISCUSSION

Dr. Marion B. Sulzberger, New York: I feel called on to make some explanation of the passage from the "Year Book," which Dr. Hazen was kind enough to quote. I think all serologists are in agreement today that the precipitation and complement fixation reactions produced by syphilis are true antigen-antibody reactions. In order to understand this, one may have to invoke the theory of heterogenetic antigens: that the products of certain macro-organisms or micro-organisms may produce antibodies which enter into reaction with products of other apparently unrelated organisms. It is possible to explain the Wassermann reaction on other theoretical grounds, which I will not go into here. However, on the basis of the heterogenetic theory, one may assume that the lepra bacillus, the plasmodium of malaria and the spirochete of syphilis contain such antigens.

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14. Wise, Fred, and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1936, p. 495.

All the serologic reactions would then be true antigen-antibody reactions. However, there are doubtless false precipitation reactions which are based not on the interplay of antigen and antibody but on a disturbance in colloidal and physical states which leads to a precipitation. Witebsky and his collaborators have worked out a type of test to decide whether the precipitation obtained is a true antibody reaction or simply the result of a disturbance in physicochemical equilibrium. As I understand it, the simplest possible explanation of this test is as follows: If one takes the precipitate which is formed and redissolves it, the solution of that precipitate contains no antibody, provided the precipitate was not due to an antigen-antibody reaction; but if one takes the precipitate which is produced by a true antibody reaction and redissolves it, one again gets the antibody and can again obtain positive results from a precipitation test with it. This "confirmation test" of Witebsky was worked out, I understand, in leprosy. The results would correspond with the committee's findings, for it has shown that the reaction in leprosy is not a true antigen-antibody reaction such as that obtained in syphilis. The reaction in leprosy is based on a physicochemical mechanism of precipitation and is not produced by the presence of an antibody. Dr. Witebsky is my source for the preceding statements; he is now in Buffalo. I believe he will be glad to furnish the essayists with much more accurate information than I am capable of submitting.

Dr. Paul A. O'Leary, Rochester, Minn.: I wish to record among the cases in which there were false positive reactions those of a group of young women who had positive reactions to precipitation tests during the menstrual period. Some of these women were employees of the clinic, so I have had an opportunity to watch them for some time. Although the likelihood of syphilis has been eliminated in connection with these women, the positive reactions which are present only during the menstrual period have been difficult to explain.

In relation to false positive Wassermann reactions, it seems to me that the more these newer serologic tests are used, the more difficulty there will be in interpretation of some of the weakly positive reactions. Dr. H. S. Sanford has been performing the Kline, Hinton, Kahn and Kolmer tests at the clinic for several years, and at first I thought that problem had finally been solved. I find myself now more confused in the matter than I was several years ago. The weakly positive tests obtained repeatedly from different laboratories for apparently healthy young adults with no history of exposure and not even circumstantial evidence of congenital syphilis cause much concern to the clinician. I am of the opinion that the serologists who are doing sensitive precipitation tests will either return to doing the more conservative type of test or develop a test with a higher degree of specificity.

Dr. A. W. Stillians, Chicago: I am glad to hear Dr. O'Leary make that statement, for it expresses the opinion I have held for some time.

I was much interested in the paper. I doubt that it will be possible to get a perfect serologic test. Certain syphilitic patients, no matter how carefully exclusion tests are employed, will still have negative reactions.

Dr. F. E. Senear, Chicago: As Dr. Hazen indicated in the paper, it is certainly to be hoped that some acceptable method will be devised for differentiating these falsely positive reactions. The committee for evaluation attempted in the first study to exclude a number of factors which have been thought to cause many falsely positive reactions. In that study the group of cases of the different diseases was too small to permit any definite conclusions. For that reason this special study in malaria was undertaken, and it would seem from the findings

that malaria is capable of producing a falsely positive reaction in some cases. My associates and I were familiar with the work of Witebsky through the quotation given in the paper, but consultation with serologists in this country would indicate that no test yet has been proved definitely acceptable.

There was no way of checking the Wassermann reaction after malaria therapy, but in most instances the falsely positive reaction disappeared in a relatively short time.

I think every one is in accord with the statements of Drs. O'Leary and Stillians that the situation is complex. Dr. O'Leary spoke of the influence of the menstrual period. I have seen a young woman for whom repeated tests by different laboratories on the same day gave results varying from frankly negative to strongly positive when comparable specimens of blood were used. The patient herself had noted that the strongly positive reactions were obtained at the time of the menstrual period, and I was interested to hear that Dr. O'Leary has observed that association. In the first study specimens were taken during the menstrual period, and there was nothing to indicate that the menstrual period had any effect.

A short time ago Vaurs listed some sixty-seven serologic tests for syphilis, and he apologized for the incomplete list. With any such number it is obvious that there will be variations in results, for the tests vary so markedly in sensitivity in individual instances.

Our purpose in this paper was to indicate that malaria may be set aside as one disease which is capable in certain instances of producing falsely positive reactions.

DERMATITIS DUE TO COCOBOLO WOOD

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Cutaneous irritation due to handling of various woods is well known to dermatologists. Senear [1] in his masterly discussion gave a complete list of woods that have been causative agents in contact dermatitis.

Cocobolo wood as a cause of persistent contact dermatitis was first reported by MacKee.[2] Although this report preceded the advent of the modern patch test, the clinical history is so clear that there can be no doubt that contact with cocobolo wood was the cause of the eruption. White [3] in his classic book on occupational diseases mentioned cocobolo wood as a cause of dermatitis. More recently, Modlayr [4] proved by the patch test that cocobolo was the cause in a case of dermatitis.

Cocobolo wood, grown in the tropics, has many uses owing to its being heavy and rugged. It is employed in making articles such as knife handles, bowls and walking sticks, in which strength is a prime requisite. The color of cocobolo wood is a rich reddish brown, and the wood has a beautiful grain when polished.

The agent probably responsible for the dermatitis is an ether-soluble resinous oil. This can be obtained easily by soaking cocobolo sawdust in ether. The solution is then filtered, and the ether allowed to evaporate, leaving in the dish a dark brown gummy substance with a pungent odor. MacKee [2] expressed the belief that this substance is closely related to the oily irritant substance in Rhus toxicodendron.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University; Director, Dr. George M. MacKee.

1. Senear, F. E.: Dermatitis Due to Woods, J. A. M. A. **101**:1527 (Nov. 11) 1933.

2. MacKee, G. M.: Dermatitis Venenata from Cocobolo Wood, J. Cutan. Dis. **31**:582 (Aug.) 1913.

3. White, R. Prosser: The Dermatergoses, or Occupational Affections of the Skin, ed. 4, London, H. K. Lewis & Co., Ltd., 1934, p. 369.

4. Modlayr: Palisander oder Cocoboloholz Dermatitis, Zentralbl. f. Haut- u. Geschlechtskr. **36**:728 (April 5) 1931.

REPORT OF A CASE

H. L., a man aged 42, was admitted on March 12, 1937, to Dr. Isadore Rosen's dermatologic service at the New York Post-Graduate Medical School and Hospital, with a cutaneous eruption of four months' duration. It was limited to the face, the scalp, the neck, the arms and the backs of the knees. Pronounced erythema, scaling and exudation of serum were present.

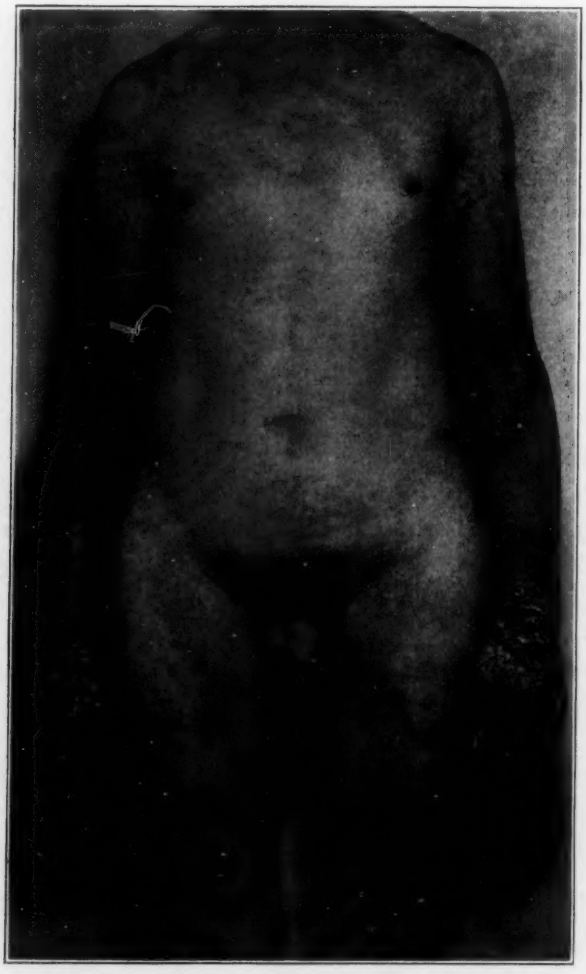

Fig. 1.—Dermatitis due to cocobolo wood.

No familial allergic tendencies were noted in the history, the patient's present cutaneous disease being his first. However, he did state that he had some scaling in his scalp, a greasy skin and a tendency to profuse perspiration.

His work necessitated his exposure to many kinds of dust, since he was a clerk in a stock-room.

The eruption had appeared four months previously, when he began to carve a handle for a knitting bag from cocobolo wood. His face soon showed intense

edema. As he did not realize the cause of his trouble, he tried several times to finish the handle—hence the development of the severe dermatitis described. The eruption was especially severe on his hands. The patient was never able to finish the handle.

The history was so clearcut that patch tests were made with cocobolo sawdust. In twenty-four hours, at the site of the test there was marked erythema with vesiculation and edema. Patch testing was done with the dust of the stock-room where the patient worked, and this resulted in slight erythema and vesiculation. It was later ascertained that cocobolo sawdust was a component of this dust.

An ethereal extract was prepared from cocobolo sawdust. Patch testing with this oil resulted in marked erythema, edema and vesiculation. Patch tests with mahogany and white pine gave negative results. These materials were used because the patient handled them.

Three patch tests were made with cocobolo wood or its ethereal extract, to confirm the diagnosis. A general flare-up of the eruption took place on each occasion.

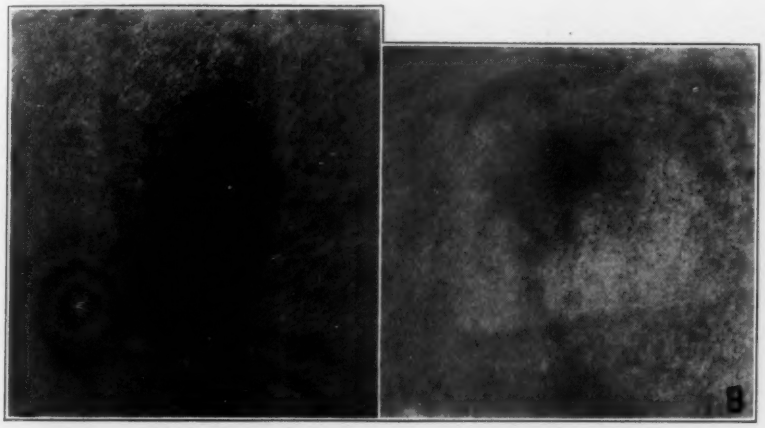

Fig. 2.—*A*, site of patch test with cocobolo sawdust. *B*, site of patch test with ethereal extract of cocobolo wood.

After the diagnosis was definitely established and patch testing stopped, the eruption gradually cleared under mild topical applications. The patient was discharged nineteen days after admission, at which time his eruption had practically disappeared.

SUMMARY

A case of dermatitis proved to be caused by cocobolo wood is reported. The patient had the background of seborrhea and the sweating tendency predisposing him to cutaneous irritation. Positive results were obtained from patch tests with both cocobolo sawdust and an ether-extracted oil from the same material. A general flare-up of the eruption was noticed in connection with the patch testing. Removal of the patient from contact with cocobolo wood and mild topical applications eventuated in recovery.

853 Seventh Avenue.

MESENCHYMOMA

A NEW TYPE OF TURBAN TUMOR

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The study of the rather uncommon tumors of the scalp continues to be interesting and, unfortunately, confusing. The confusion comes chiefly from the group of nonepitheliomatous tumors, which includes especially atypical sarcoma and the so-called endothelioma. In cases in which such a condition is present we believe it is preferable to describe only the morphologic picture and to omit personal interpretations. In this way the more important clinical aspects, as regards appearance, prognosis and therapy, can be evaluated critically. It is necessary, of course, to include extensive histologic analyses, so that the morphologic study may be as complete as possible. Naturally, the opinion of the trained oncologist is required. The case we shall describe illustrates well the problems which confront the student of tumors of the scalp.

REPORT OF CASE

T. G., a Negro aged 47, a porter, first noticed in 1926 or 1927 a small (2 cm.) hard subcutaneous tumor on the right parietal area of the scalp; the hair was lost over this tumor. According to the patient, the size of this tumor varied considerably; at times it definitely disappeared (?). In 1929 a similar lesion appeared in the same area; this tumor also varied in size. In 1931 ulceration and fistulous tracts developed in the region. The scalp enlarged gradually, until the entire area was involved. The swelling spread slowly down over the face, and paralysis of the left side of the face became evident. The patient began to complain of some heaviness of the head and some difficulty in hearing. There was no history, either personal or familial, of syphilis, tuberculosis or a malignant growth. Likewise no member of the family had had a tumor of the scalp. The patient was referred to the dermatologic department of the Cincinnati General Hospital by one of us (Dr. Barrett).

On admission to the hospital the patient presented a diffuse enlargement of the entire scalp, with the greatest circumference measuring 75 cm. The hair was sparse. A definite firm edge of the enlargement was observed about the eyes and

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the ears. In the occipital area were two 4 cm. ulcers covered with a dirty red granulomatous base. There was superficial paralysis of the left side of the face. The scalp felt soft and rubbery and was painless. Small, discrete, painless submental and postauricular glands were palpable. The pupils were equal, regular and active. The eyeballs and the fundi were normal. The auditory meatuses were almost entirely closed by swelling, and auditory acuity was markedly diminished. The thyroid gland was not enlarged. The heart and the lungs were normal. No viscera were palpable in the abdomen. The penis was normal. The neurologic examination showed no abnormality except on the face. Roentgenograms showed no involvement of the bones of the scalp and old interlobar pleurisy of the right lung. No bony changes were seen. The urine was normal. The blood count revealed 16,000 white cells, 5,200,000 red cells and 82 per cent hemoglobin (Sahli); the differential count showed 35 per cent lymphocytes, 48 per cent polymorphonuclears, 1 per cent basophils, and 16 per cent mononuclears and transitional forms. No abnormal cells were found on repeated smears. Tests with human and bovine tuberculin (0.1 mg.) gave negative results. Smears of tissue showed no organisms with various stains, including stains for acid-fast bacilli. Cultures on various mediums produced only Staphylococcus aureus. Cultures of blood showed no organisms.

The tumor continued to grow in all directions. The surface of the skin became dark brown. The mass became less firm, but there were no areas of definite fluctuation. Other fistulous tracts appeared throughout the scalp. No marked cervical adenopathy developed. It was extremely difficult for the patient to eat, and his headaches became nearly intolerable. The patient had no febrile periods until the onset of pneumonia. He received, in addition to the usual general measures, intravenous injections of typhoid vaccine and one minute exposures of the entire scalp to roentgen radiation at a 12 inch (30.5 cm.) skin-target distance with a 1 mm. aluminum filter, 110 kilovolts and 3 milliamperes. Some six weeks after admission the patient died of lobar pneumonia and cachexia.

Section by Dr. Ralph Fuller three hours after death showed the scalp to be from 5 to 7 cm. thick and the subcutaneous tissue pale yellow and elastic. The soft calvarium was normal. There was one soft, gray, gelatinous swelling at the junction of the costal cartilage and the sternal end of the seventh rib on the left. No additional metastases could be found grossly. There was pneumonia of the lower lobe of the right lung. The kidneys had a mottled appearance. Microscopic sections of the tumor showed the skin and the subcutaneous tissue to be invaded by tumor cells. These cells were large and undifferentiated and had a large oval or round nucleus, which was rich in chromatin, and frequently a nucleolus. The cytoplasm of these cells was pale. Special staining with the Van Gieson stain and stains for reticulum (Foot and Foot) revealed an intertwining network of short cytoplasmic processes. No definite relation of these cellular masses to blood or lymph vessels or other structures could be seen. Chronic inflammation was observed in some areas. The metastatic nodule revealed the same histologic picture. A few tumor cells were found in the stroma of the right kidney. Many of the tumor cells were pyknotic. That this condition was not due to the roentgen therapy was shown by these pyknotic cells in the costosternal and renal metastases.

To summarize: This middle-aged Negro presented a peculiar tumor of the scalp of six years' duration. The tumor began as a few discrete nodules and later became diffusely invasive and productive of metastases. The tumor apparently caused considerable lymphedema of the scalp. The microscopic picture is necessary for the identification of the tumor, and this study brings up an old controversy on endotheliomas in general and tumors of the scalp in particular.

In 1869 Golgi [1] introduced the concept of epithelioma in a discussion of the structure of psammoma. Since that time speculation in regard to the existence of such a class of tumors has been extensive among pathologists. Today Ewing [2] and Kaufmann [3] have accepted the term "endothelioma." Ewing [2] defined endothelioma as "a confusing class applying to tumors of lining cells of blood vessels, lymph vessels and spaces, subdural spaces and serous cavities." Kaufmann [3] discussed the controversial question of endotheliomas and sarcomas.

> Histogenetically, endotheliomas belong to the connective tissue tumors, and in their structure are similar both to their typical representative, those poor in cells, and to the atypical, i. e., the cellular sarcomas; which means that some are benign like fibromas, and most of the dural endotheliomas, and some are malignant like sarcomas which include many blood vessel endotheliomas as well as some endotheliomas of serous membranes. Nevertheless, "cellular" and "malignant" are not in themselves synonymous, and therefore cellular endotheliomas cannot be generally and simply called sarcomas, i. e., endothelial sarcomas, to include the clinical conception of malignancy, because some endotheliomas, as in the meninges, may be very cellular and yet benign in their relationship. For this reason the author would continue the formal separation of endothelioma from sarcoma in a histological sense.

For the dermatologist the question of endothelioma has a special interest, chiefly by reason of a certain peculiar group of tumors of the scalp described first by Ancell [4] and later more fully and definitely by Spiegler.[5] Today this tumor is mentioned usually as "endothelioma of Spiegler." The clinical picture of this tomato-like tumor of the scalp is well known and will not be repeated. However, it appears not to be well understood that these tumors may be familial (three generations in Ancell's cases), occasionally ulcerative and even rarely metastatic. The metastases were not proved in one of Ancell's cases, since microscopic sections of the supposedly involved abdominal viscera were not made. Because of the controversy in regard to endothelioma, these tumors have received names of all sorts, the latest contribution being the one of Kogoj,[6] naevus epitheliomato-cylindromatosus.

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1. Golgi, Camillo: Sulla struttura e sullo svillapo degli psammomi, Pavia, 1869; abstr., Virchows Arch. f. path. Anat. **51**:311, 1870.

2. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

3. Kaufmann, Edward: Pathology for Students and Practitioners, translated by Stanley P. Reimann, Philadelphia, P. Blakiston's Son & Co., 1929, vol. 1, p. 183.

4. Ancell, Henry, cited by Spiegler.[5]

5. Spiegler, Edward: Ueber Endotheliome der Haut, Arch. f. Dermat. u. Syph. **50**:163, 1899.

6. Kogoj, F.: Ueber das Verhalten des Hyalins in Cylindromen, Arch. f. Dermat. u. Syph. **166**:515, 1932.

The careful studies of Spiegler [5] and Haslund [7] of tumors of the scalp and the reports of Gottheil,[8] Juliusberg [9] and Wise [10] of generalized endothelial tumors have given excellent descriptions of these conditions. The interpretation is the cause of all the controversy. The quarrel of the general pathologists has spread, naturally, to the dermatopathologists.

By 1899 Spiegler [5] had already introduced the element of doubt:

> But these tumors are in many respects interesting histologically on account of their peculiar structure, and on account of the difficulties which arise on an attempt to classify them.

Again, after his study of many serial sections, he claimed:

> I was unable to show a connection with any definite blood vessels. Therefore, I can assume only theoretically (hypothetically) that the tumors arise from the endothelia of the lymph spaces.

Ewing [2] expressed doubt of the endothelial origin of the condition in Haslund's case, and apparently Haslund [7] did too:

> I am far from believing that I have even solved the problem of these tumors which are perhaps not of a homogenous genesis [origin]. [He means that it is uncertain whether the tumors actually arise from the endothelium of the lymph spaces.] Many questions I had to answer with the answer so frequent in medicine: "We do not know."

Unna [11] stated that he did not believe the endothelioma to be a separate and distinct type of tumor of the skin. Ziegler [12] expressed the belief that there are no sharp limits between endothelioma and sarcoma and that, on the contrary, transitional forms are present. Darier [13] reserved for the peculiar tumor of the scalp of Spiegler [5] the term "cylindroma," an epithelioma generally of basal cell type the stroma and even the epitheliomatous tissue of which undergo a form of mucous and hyaline degeneration or cylindromatization. Busman,[14] from a study of "malignant" endothelioma, claimed: "The size of the growth

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7. Haslund, Poul: Multiple Endotheliome der Kopfhaut, Arch. f. Dermat. u. Syph. **82**:247 and 324, 1908.

8. Gottheil, W. S.: Endothelioma of the Skin, J. A. M. A. **48**:931 (Jan. 12) 1907.

9. Juliusberg, Fritz: Lymphangio-Endothelioma cutis abdominis, Arch. f. Dermat. u. Syph. **89**:77, 1908.

10. Wise, Fred: Multiple Endotheliomas of the Skin, Am. J. M. Sc. **157**:236, 1919.

11. Unna, cited by Haslund.[7]

12. Ziegler, cited by Haslund.[7]

13. Darier, J.: Précis de dermatologie, ed. 4, Paris, Masson & Cie, 1928.

14. Busman, George J.: Malignant Endotheliomas with Cutaneous Involvement, Arch. Dermat. & Syph. **6**:680 (Dec.) 1922.

at the time of study makes it practically impossible to trace the various cells through their transition stages to the original proliferating endothelium."

Other types of primary tumor which are considered usually in the differential diagnosis of this type of tumor of the scalp are sarcoma, lymphosarcoma, carcinoma—chiefly multiple benign cystic epithelioma, adenoma sebaceum (Civatte) and tricho-epithelioma—sebaceous cysts, with and without degeneration, and nevi.

Ronchese [15] has reported multiple "benign" epithelioma of the scalp in a father and his daughter. Reticulo-endotheliosis, or more specifically for this case aleukemic reticulosis, was also a possibility, but the histologic studies ruled this out.

With these various differential diagnoses, with the confused concept of endothelioma and with the warning of Ewing [2] that "the personal impressions of the individual observer have figured too prominently in the steady expansion of this group of tumors," we feel that the picture in our case can fit into none of the classes mentioned. The important point in diagnosis is the differentiation of the condition from the tumor of the scalp described by Spiegler. The tumor in this case was diffusely invasive, fairly rapidly growing in its later period and distantly metastatic. Most important are the different histologic pictures. In our case there were none of the supposedly epithelial characters of the cells and likewise no cylindromatization. Moreover, there were no "translucent polyhedral cells, with pale nuclei devoid of acidophilic nucleoli," and no "relation to blood vessels." Ewing [2] claimed "definite formation of intercellular fibrils I have been unable to detect in endothelioma." Yet stains of the reticulum in our case showed a fine meshwork in the areas affected by tumor. The tumor cells were likewise too young and too undifferentiated to warrant a diagnosis of sarcoma. Nékám,[16] however, after examination of the sections in this case, proposed the diagnosis of polymorphocellular sarcoma.

In the present state of knowledge of classification, we can say with Haslund,[7] *"ignoramus."* In spite of the objections of Ewing [2] to an embryonal classification, at the present we must be satisfied with calling the growth an undifferentiated malignant tumor of mesenchymal origin, a mesenchymoma. Rather than put doubtful and confusing tumors into definite classes and so disturb the clinical concepts of the tumors of these classes, we believe that we should not conceal our ignorance. We should indicate merely that such tumors are so young and so undifferentiated that we can say no more than that they are of mesenchymal origin. Because of these doubts, the term mesenchymoma has been

15. Ronchese, F.: Multiple Benign Epithelioma of the Scalp (Turban Tumors), Am. J. Cancer **18**:875 (Aug.) 1935.

16. Nékám, Louis: Personal communication to the authors.

applied before by Austin [17] and by Foot,[18] and we adopt it for this new type of turban tumor of the scalp. We believe that we are not adding to dermatologic verbosity by offering such an "emergency" term of the general pathologist to the dermatopathologist but are merely serving to differentiate more clearly certain classes of tumors. This term does not invalidate the concept of true endothelioma. "Mesenchymoma" merely takes away from "endothelioma" many dubious, distant relatives. The use of an embryologic term is not of merely academic interest, because the tumor in this case has been diagnosed variously by pathologists and dermatopathologists as epithelioma, sarcoma and endothelioma. For just this reason a new class is needed for such tumors. The term is indefinite and not limited, but sarcoma and epithelioma—and perhaps even endothelioma—are fixed and known classes. The volume of tumors classified as mesenchymoma will be inversely proportional to increasing advances in oncology.

SUMMARY

A middle-aged Negro with a new type of primary tumor of the scalp is presented. The tumor was highly invasive locally and gave rise to metastases to the ribs and to the kidneys. Careful study of the tumor cells does not warrant inclusion of the condition in any of the usual classifications of tumors. Because the tumor cells were so young and so undifferentiated, the term "mesenchymoma" is applied to this type of malignant tumor of the scalp.

ABSTRACT OF DISCUSSION

DR. ERICH HOFFMANN, Bonn, Germany (by invitation): In my opinion this condition is different from Spiegler's tumor of the scalp because it is granulomatous and malignant. I have examined the patients whose cases were reported by Spiegler (material received from Prof. A. Riehl), Haslund, Juliusberg and others as well as one of my own for whom the connection with naevus tricho-epitheliomatosus could be proved. Such tumors are chronic and characteristic, because their origin from the deeper layers of the hair follicle can be demonstrated by the presence of a hyaline membrane originating from the membrana hyaloidea of the normal hair follicle. This kind of "turban tumor" was described in a book by W. Frieboes (Beitrag zur Klinik und Histopathologie der gutartigen Hautepitheliome, Berlin, S. Karger, 1912) and by me at the International Dermatologic Congress in Rome in 1912 (*Deutsche med. Wchnschr.* **36**:2365, 1910).

DR. S. E. SWEITZER, Minneapolis: I am sorry Dr. Tauber used the term endothelioma for this tumor. Dr. Winer and I recently published a paper on this condition, which is a vascular tumor, but I think no one can recognize the endothelial cell unless he sees the inside of it.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I agree with the previous discussers that this condition is not naevus cylindromatosus (cylindroma or endothelioma capitis), epithelioma adenoides cysticum or syringoma. All the latter conditions may be closely related, as was recently shown by Ingels (ARCH.

17. Austin, R. S.: Personal communication to the authors.

18. Foot, N. C.: Personal communication to the authors.

DERMAT & SYPH. **32**:75-85 [July] 1935). In Dr. Tauber's case one is apparently dealing—if I may judge from his lantern slides—with a malignant grade 4 cancer starting in the skin and involving the internal organs secondarily. On the other hand, I have observed two cases in which multiple tumors in the scalp were misdiagnosed as carcinoma of the sweat glands when actually they represented metastatic lesions from the kidneys in one case and from the gastro-intestinal tract in the other. Histologic diagnosis of Dr. Tauber's slide by different pathologists might vary, but the numerous mitotic figures present show it to be definitely a growth of grade 4 malignancy. Studies of the blood apparently would rule out the various leukemias, except for their aleukemic phases. I do not think the condition in Dr. Tauber's case is one of true adenosarcoma of the sweat glands. Sarcoma of grade 4, especially lymphosarcoma, is a possibility.

DR. DAVID L. SATENSTEIN, New York: According to the history, a nodule of the scalp appeared and disappeared, and ulceration spread over the scalp. This history, together with the microscopic picture of the lesions of the scalp and the lesions of the kidney, make me believe the condition is mycosis fungoides that started as a tumor. The finding of the network fits in well with the mitoses. I should suspect mycosis d'emblée.

DR. FRED D. WEIDMAN, Philadelphia: When I first read the abstract of this paper I surmised that this condition was essentially tricho-epithelioma of the scalp, a lesion which may or may not be associated with lesions of the face. I was influenced in that direction by the fact that Dr. H. L. Traenkle has recently studied a full series of such cases in my laboratory and, I think, has established the fact, long claimed but not sufficiently advertised, that the Brook type of epithelioma may appear on the scalp and is essentially a tricho-epithelioma. I am satisfied that that was not the condition of Dr. Tauber's patient. Dr. Satenstein anticipated me. I am convinced that it was one of the lymphoblastomas. Studies of the blood have ruled out the leukemic types, leaving perhaps mycosis fungoides, but at any rate one of the aleukemic lymphoblastomas. I feel that further studies will place this condition among the essential diseases of blood-forming tissues. It is true that the infiltrations have been comparatively localized to the scalp, the costo-clavicular junction and the kidneys, but after all, the localization of tumors of the blood-forming tissue is not at all regular.

It is not clear to me whether the patient had generalized lymphadenopathy—clinically speaking—or whether the tumescences were confined to the tumor. I hope Dr. Tauber will make that point a little clearer when he closes the discussion.

DR. ELMORE B. TAUBER, Cincinnati: I thank the discussers for their remarks. When this case first came under observation we tried to find some diagnosis to fit this type of tumor. Frankly, at first we did not think, as we are beginning to now, that the condition belonged in the lymphoblastoma group and was of the type the members have all seen many times, consisting of fixed patches that persist for a long time and eventually become mycosis fungoides. I agree with Dr. Hoffmann that this tumor does not fit in with tricho-epithelioma.

The reason we discussed endothelioma of Spiegler was that we wished to differentiate this condition from that type of lesion.

Dr. Satenstein and Dr. Weidman, I think, possibly have come close to the group in which this condition will finally be placed. That was why we attempted at the outset to name it before we found out exactly where it belonged, calling it mesenchymoma until time would let us arrive at a definite diagnosis. As Dr. Satenstein brought out, there is evidence of its resembling mycosis fungoides. There was only some cervical adenopathy, which could probably be differentiated from this tumor material.

PATHOGENESIS OF NONCASEATING EPITHELIOID TUBERCULOSIS OF HYPODERM AND LYMPH GLANDS

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AND
RALPH R. MELLON, M.D.
PITTSBURGH

In a previous report by us [1] there was developed a new conception of the bacteriologic characteristics and the pathogenesis of noncaseating epithelioid tuberculosis, which was based on new biologic experiments with the tubercle bacillus. Briefly, the import of these studies was that during the life of the tubercle bacillus it assumes several nonacid-fast or partially acid-fast forms, which at present are included in wholly different taxonomic categories of bacteria, such as streptotrichotic forms, diphtheroids and certain cocci.

The proof of this contention lies in the fact that we have observed the dissociation of tubercle bacilli into such organisms and, on occasion, their reversion into the original tubercle bacilli. Moreover, these cultural phases are more or less interchangeable. On the other hand, their stability is relatively great, and the changes are effected only with difficulty.

It is the latter circumstance that explains in part the bacteriologic anomalies of noncaseating epithelioid tuberculosis—that is to say, the presence of these relatively nonvirulent and nonacid-fast dissociants of the tubercle bacillus and the absence of the latter either culturally or by animal inoculation represent, in brief, the findings in this peculiar clinical condition. We may represent the streptothrix as culture phase 1, the diphtheroid as phase 2 and the micrococcus as phase 3. In a single case all of these may be isolated, or only one or two of them may be present.

In a case observed in this laboratory and reported by Crawford,[2] phases 2 and 3 were present, while in the recent study reported by us [1] only phase 1 was found. The fact that it was transformed into an acid-

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Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., June 3, 1937.

1. Mellon, R. R., and Beinhauer, Lawrence G.: The Pathogenesis of Noncaseating Tuberculosis of the Skin and Lymph Glands, Arch. Dermat. & Syph. **36**:515 (Sept.) 1937.

2. Crawford, Stanley: Cutaneous Nodulodiscoid Tuberculosis of Anergic Type with Development into Active (Allergic) Pulmonary Tuberculosis, Arch. Dermat. & Syph. **27**:766 (May) 1933.

fast organism recognizable as a dissociant of the tubercle bacillus proper gave special significance to its presence. In the case under consideration in this paper we shall report the presence of phase 2 alone. In addition, the pulmonary picture in this case was so unusual as to require reconciliation on some other ground than that of conventional tuberculosis.

The characteristic absence of allergy to old tuberculin manifested in such cases makes it likely that the original infection is brought about by a hitherto unrecognized dissociant (variant) of Koch's bacillus. This point of view was supported in our previous paper by two considerations: first, the transformation of the partially acid-fast streptotrichotic form (obtained in pure culture from the lesions) into a rough-colonied variant of the tubercle bacillus; second, the experimental production in guinea pigs' lungs of noncaseating epithelioid lesions which did not result in progressive fatal tuberculosis. Of additional significance is the fact that this rough variant—quite distinct in its characters from the "roughs" of Petroff, Kahn and others—produces a tuberculin sufficiently different from that of Koch's bacillus to produce a reaction in certain of the anomalous cases under discussion.

In other words, our theory would predicate initial infection in these cases by the critical rough form (or some closely related dissociant of Koch's bacillus) in a hypersusceptible host such as the Negro is known to be. After production of the lesions, however, the organism becomes dissociated into one or more of the three nonacid-fast culture phases, which serve, perhaps, to keep the infection alive in a low grade form.

This theory would explain the reaction of the patients to the special tuberculin of our critical R form, their failure to react to Koch's old tuberculin from any of the three types of the Koch bacillus and the almost universal failure of animal inoculation to produce progressive tuberculosis, to say nothing of the impossibility of isolating the Koch bacillus by culture. Finally, the termination of the condition in conventional pulmonary tuberculosis in some of the cases is readily explained by the reverse dissociation of some of these strains to Koch's bacillus per se. One of us (R. R. M.) reviewed the highlights of a case [3] in which just these sequences were proved, but its details have been reserved for a subsequent communication.

REPORT OF A CASE

R. C., a Negro aged 38, presented himself at the Falk Clinic of the Pittsburgh Medical Center on Dec. 2, 1935, because of a mass on the left palm. The patient stated that the lesion appeared in May 1935, three months after he had opened an ulcer on the udder of a cow which he milked daily. The lesion developed insid-

3. Mellon, R. R.: The Newer Biology of the Tubercle Bacillus: Its Variability, Filtrability, and Life-Cycle Changes, in Goldberg, B.: Clinical Tuberculosis, Philadelphia, F. A. Davis Company, 1935, chap. 11.

iously as a small nodule and gradually enlarged, becoming painful. He sought medical advice, and the lesion was excised in November 1935 but promptly recurred.

Examination revealed a sharply defined, fibrotic, firm nodule, the size of a dime, on the palmar surface of the left hand. It lay unattached, directly over the tendon, near the base of the second finger. The lesion was painless on pressure. The adjacent epitrochlear lymph gland was enlarged to the size of an olive, discrete in outline and painful to pressure. A similar, somewhat smaller lymph gland was present in the right epitrochlear region, and a small amount of generalized adenopathy was present. The palmar mass was removed, and roentgen therapy was applied to the affected area, but a complete recurrence was noted within three months.

The patient was then admitted to the hospital, on April 22, 1936. There was no history of tuberculosis in the family. The patient had had measles and whooping cough in childhood, had undergone tonsillectomy in 1925 and had had influenza in 1929. Gonorrhea was contracted in 1933, but the patient stated that he had not had syphilis.

About January 1935, an afebrile "cold" was contracted and was followed by a hacking cough, producing occasional yellowish lumpy sputum but no evidence of blood. A referred substernal pain, aggravated by deep inspiration, developed and lasted for three weeks. The physical examination at that time showed no abnormality, and repeated examinations of sputum revealed no tubercle bacilli.

The patient was free from subjective symptoms until the appearance of the palmar lesion, in May 1935, when a nonproductive cough and pains in the right side of the chest appeared, accompanied with an afebrile reaction. Again tests of the sputum and physical examination showed no sign of tuberculosis. Strapping of the chest gave complete relief, and the patient returned to his work. During the previous year a loss of 16 pounds (7.2 Kg.) of body weight was noticed, and progressive weakness and fatigue were apparent. The weight was regained, and the subjective symptoms cleared after the removal of the enlarged lymph glands and the palmar lesions.

Physical examination showed a well developed man weighing 154 pounds (68.2 Kg.) and experiencing no apparent distress. The pupils were equal and reacted normally. The nose and the throat showed no abnormality. The teeth were in excellent condition. The liver and the spleen were not palpable. The examination of the chest revealed that the expansion of the right lung was slightly decreased. There were areas of impaired breathing and resonance. No rales were heard during coughing. (A note by the internist stated that even though the roentgenograms showed definite mottling, the physical signs would not permit a diagnosis of active tuberculosis, for a Negro with active or quiescent tuberculosis of the lungs would be expected to show signs of symptoms—or even some clinical progress—of the disease.)

The heart showed normal size and rhythm, and there was no evidence of pathologic change. The right supraclavicular region revealed one large and numerous small shotty glands. The blood pressure was 120 systolic and 80 diastolic; the pulse was regular, with a rate of 84 per minute, and the temperature never exceeded 98.2 F. The prostate was soft and even and gave no evidence of pathologic change. The genitalia were normal.

There were 4,340,000 red blood corpuscles, 6,300 white blood corpuscles and 90 per cent hemoglobin. The differential count revealed 60 per cent polymorphonuclears, 16 per cent small lymphocytes, 16 per cent transitional forms and large

mononuclears and 8 per cent eosinophils. The urine revealed no albumin or sugar, no casts, a specific gravity of 1.024 and from 20 to 30 white blood cells under high power magnification. The Wassermann and the Kahn reaction were negative. The prostatic smear revealed many clumps but no intracellular diplococci or tubercle bacilli.

Lumbar puncture and a Kahn test gave negative results. Avian, bovine and human tuberculin, with dilutions of 1:1,000 produced negative reactions; critical R tuberculin, with a dilution of 1:10,000 produced a red, moderately indurated reaction 5 by 5 mm. This reaction was present only after the recovery of an acid-fast, avirulent bacillus in the sputum. Weekly examinations of sputum from April 22 to Oct. 10, 1936, showed no tubercle bacilli but revealed an occasional fusiform bacillus and a few spirilla. During iodide therapy, from Oct. 10 to Oct. 20, 1936,

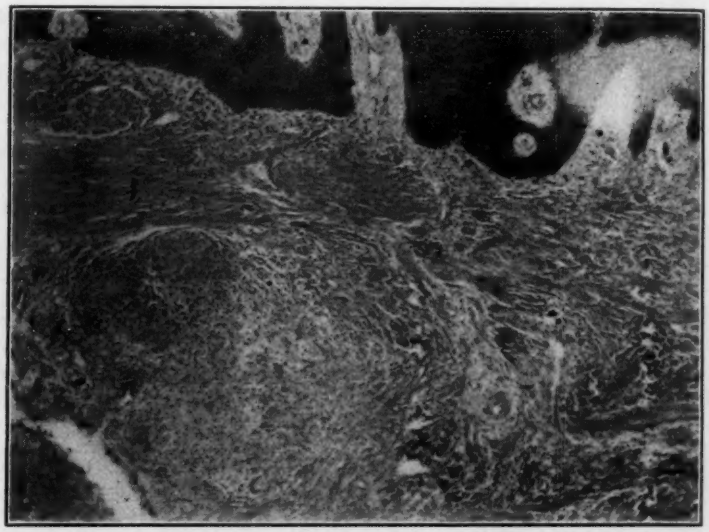

Fig. 1.—Photomicrograph of a section from a palmar lesion, showing discrete miliary and conglomerate noncaseating epithelioid tubercles.

an acid-fast bacillus indistinguishable morphologically from the tubercle bacillus was observed in the sputum, but results of all cultures were negative. Cultures of sputum showed no fungi. Repeated inoculation of guinea pigs with this organism failed to produce tuberculosis. Agglutination of serum gave no evidence of Bacillus tularensis. The tuberculin reaction of the cow which the patient had milked was negative at this time and had been for two years prior to the development of the ulceration of the udder.

Microscopic examination of the skin (fig. 1) showed the skin to be covered by a thick layer of keratin. Beneath the corium was a granulomatous reaction showing typical arrangement of monocytes, multinucleated giant cells surrounded by connective tissue and lymphocytes. The tubercles formed were both miliary and conglomerate. A small section from the deeper tissue consisted of fat through which a heavy connective tissue septum extended. In the septum was a granulomatous reaction resembling tuberculosis. There was no evidence of caseous necrosis. Sections of the lymph nodes showed a replacement of lymphoid tissue

by innumerable closely crowded nodules composed of epithelioid cells (fig. 2). In some instances these epithelioid cells showed a tendency to radial arrangement. In most instances, however, no definite arrangement of these cells was seen. Some of the nodules showed giant cells, most of them of the Langhans type. These epithelioid masses, which could be properly called tubercles, were separated from one another by thin trabeculae and in many places tended toward confluency. Caseous necrosis was not present. Some of the masses showed hyaline degeneration, and here and there lymphocytes were found in the stroma which separated the tubercles. The periphery of the lymph node beneath the capsule presented a thin margin of lymphocytic tissue. The capsule was intact.

A second mitroscopic examination from the recurrent palmar lesion showed a dense reaction of scar tissue in which a number of isolated tubercles similar to

Fig. 2.—Photomicrograph of a lymph gland, showing replacement of lymphoid tissue by innumerable closely crowded nodules composed of epithelioid cells. There is no caseous necrosis.

those described in the lymph glands were seen. Acid-fast stains and Gram stains of both sections revealed no trace of demonstrable organisms.

Roentgen examination on Dec. 23, 1935, showed the apex and the upper four interspaces of the right lung to be irregular and mottled, producing shadows of slightly positive density. A small ring shadow appeared in the center of the first interspace. The shadow of the hilus was increased and was of soft density. The left lung showed a mottled density of the second, the third and the fourth interspace and had a patchy shadow of moderate density; the appearance at the hilus was the same as that on the right.

The impression was that of a disease resembling tuberculosis or a recent infection—possibly syphilis—causing the extensive shadows of the hilus. On Feb. 11, 1936, both lungs presented a moderately dense, soft mottling. The shadows of the hili extended well into the middle zone and were dense. The left costophrenic sulcus was not distinct. The impression was that of an extensive

bilateral disease with marked involvement of the hilus, questionably tuberculosis. On April 29, 1936, examination of the chest showed an increase in the size and the density of the shadows of both hili, apparently due to glandular enlargement. There was extension from the periphery into the parenchyma of each lung. This was slightly more marked in the central zone and less advanced in the apexes and the bases. It appeared symmetrical. The diaphragm was movable on respiration, and no adhesions were noted in this region. The entire appearance was suggestive of tuberculosis, beginning in the hilar regions and extending into the lungs. On June 12, 1936, reexamination of the chest showed increased density in the upper hilar glands, on both sides, slightly more infiltration in the upper lobes and increased density in the infiltration in the middle portion of each lung.

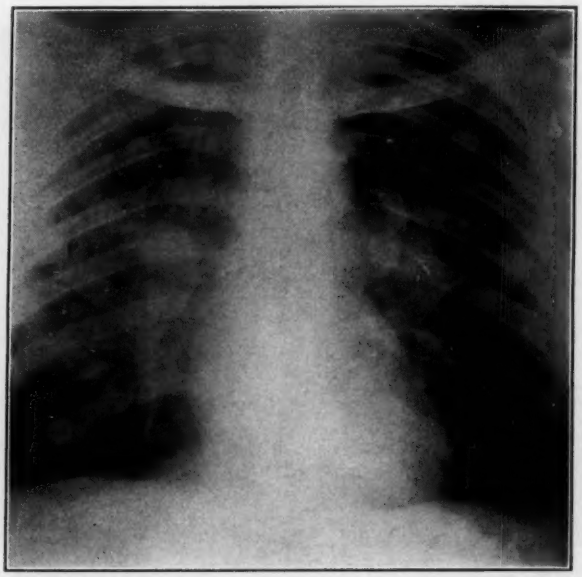

Fig. 3.—Roentgenogram showing increased density in upper hilar glands with infiltration in the upper lobes and increased density in the middle portions of the lungs.

There was no cavitation and no evidence of parenchymal destruction. Apparently the increased density was due to continued fibrosis. On Jan. 4, 1937, reexamination of the chest showed continued increase in the density and more involvement in the upper two thirds of the lungs. There was still no cavitation but more marked nodulation. The bases still remained relatively clear. The appearance was still suggestive of a generalized tuberculous infection, apparently of low grade virulence, resulting in fibrosis rather than ulceration or cavitation.

On June 8, 1937, the patient was again tested with tuberculin from our critical R strain and with Koch's old tuberculin. With the latter in 1:1,000 dilution he gave a 4 plus reaction, while the reaction to the former was negative. It will be recalled that this was exactly the reverse of the reactions obtained with these two tuberculins when the patient was first seen.

From our observation of the clinical and bacteriologic sequences in similar cases we believe that this appearance of allergy to old tuberculin coincides with a transformation in vivo of the dissociants of low virulence into bacilli of Koch. This view is supported by the fact that recently the patient has lost weight; his pulmonary lesions have become active, and he has been admitted to a sanatorium.

The roentgen examination of the bones and of the hands and the feet showed no abnormality.

On bacteriologic study of the lymph gland there was isolated a pure culture of organisms in what we have come to refer to as the sporoid cyclostage in the life history of the tubercle bacillus. Seeded on blood agar, the culture grows in a translucent, soft and rather flat small colony, the structure of which is roughly that of a diphtheroid, except that the organisms contain a variable number of

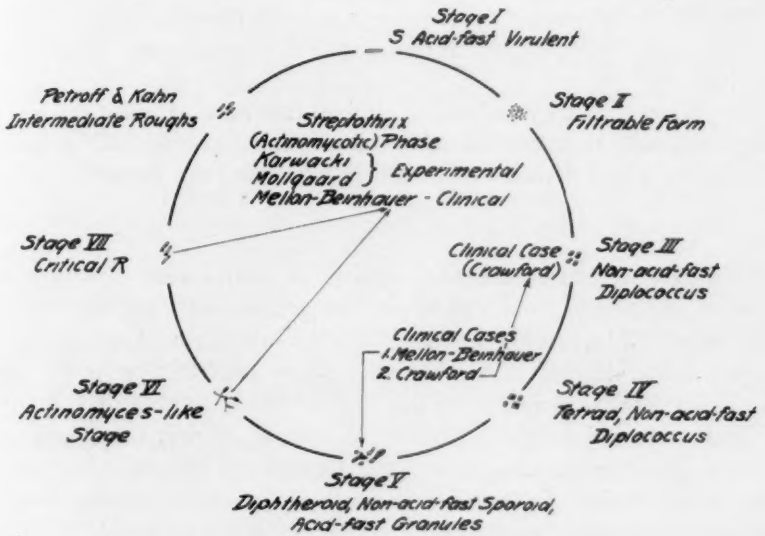

Fig. 4.—The dissociation cycle of the tubercle bacillus.

strongly acid-fast sporelike granules of varying size. Sometimes the latter may be so numerous that they occupy from two thirds to three quarters of the cell's substance, but at other times they may be relatively few. At times they give the impression of being freed from the bacillary cell. Their fancied resemblance to endospores is the reason for referring to diphtheroids of this type as sporoids.

They have been shown definitely to occupy an integral part in the tubercle cycle, having on occasion reverted to what is known as the acid-fast critical rough culture phase. No strictly acid-fast organism was isolated from the glands, nor did the material produce tuberculosis or any other pathologic lesion when injected into guinea pigs. (This was true also of the acid-fast bacillus which was found in the sputum of this patient after iodide therapy and which was indistinguishable morphologically from the tubercle bacillus.) On one occasion only a streptotrichotic form similar to that isolated and reported previously was recovered, but it persisted for only a few transfers. If it is assumed that it was entirely similar to the streptothrix isolated in our previous case, its place in the tubercle cycle would be definitely known.

SUMMARY

From the lymph glands in a case of noncaseating epithelioid tuberculosis we recovered in pure culture a diphtheroid bacillus containing strongly acid-fast granules. Because of its resemblance to an endospore we have referred to this diphtheroid as a sporoid.

This sporoid has been shown to occupy an integral part in the life cycle of the tubercle bacillus, as it was dissociated into what is known as the critical rough (R) form of the tubercle bacillus.

The patient reacted specifically to a tuberculin prepared from the critical R form when negative reactions were obtained from the tuberculins of the avian, the bovine and the human type.

No strictly acid-fast organisms were isolated from the glands, nor did the material animal inoculation produce tuberculosis or any other pathologic lesion.

From the sputum we obtained an acid-fast bacillus indistinguishable morphologically from the tubercle bacillus. The sputum on animal inoculation proved avirulent. The organism itself was not isolated.

CONCLUSIONS

The clinical and bacteriologic sequences in this case of inoculation tuberculosis support our thesis on the pathogenesis of noncaseating tuberculosis. The theory predicates that the initial infecting stage is our low virulent acid-fast (critical rough) phase, producing its own tuberculin. The patient is allergic to this but not to old tuberculin.

In this stage the disease is relatively benign, and only the nonvirulent, nonacid-fast dissociants of the tubercle bacillus are present in the lesions. The latter are indistinguishable from Boeck's sarcoid or Schaumann's benign lymphogranulomatosis. When and if these nonvirulent forms are transformed into Koch bacilli, the signs and symptoms of classic tuberculosis appear.

ABSTRACT OF DISCUSSION

Dr. Fred D. Weidman, Philadelphia: Clinically, this condition appears to start as anatomic tubercle and extend to the lymph nodes and finally to the lungs. Laboratory studies in connection with its course make the picture conform more closely, I think, to Boeck's sarcoid than to any other type of clinical tuberculosis. That is, the discussion should center around Boeck's sarcoid in relation to the bacteriologic considerations which engage the members this evening. Still, "noncaseating tuberculosis" is a term which was chosen, I take it, in order to avoid confining the designation to Schaumann's disease or Boeck's sarcoid; it has yet broader implications.

It is to the sarcoid of Boeck, therefore, as well as to Schaumann's disease, which is its twin brother, that it is proper to compare this noncaseating tuberculosis. Clinically there are similarities to Schaumann's disease, in that there were general adenopathy and pulmonary involvement. As to the bacteriologic phase, all dermatologists have suspected for a long time that there might be other organisms related to this disease; some have brought up the question of Bacillus

leprae, but most, that of the tubercle bacillus. The point of the presentation is that a precise stage has been postulated in the life cycle of the tubercle bacillus—namely, stage 5 of the authors—at which this micro-organism provokes a particular complex which approaches Boeck's sarcoid. This matter of mutation is not new. Such changes were known years ago (Much's granules) in connection with problems of tuberculosis, and dermatologists studying fungi know how closely the mycobacteria may approach the lower forms of the higher fungi, namely, Streptothrix. Some of the latter are notoriously variable toward acid-fastness and Gram's reaction; so it is not surprising that there has been discovered in the confused picture of Boeck's sarcoid a bacterium which at one stage is acid-fast and at another is not. The demonstration is the thing which has been awaited, and it is not surprising that Dr. Mellon should have made it. It may be recalled how, many years ago, Mellon became the pioneer in the work on mutation of bacteria (Weidman, F. D.: Light from the Botanic Field on Medical Mycologic Problems, ARCH. DERMAT. & SYPH. **19**:867 [June] 1929). I recall the time when he related how the colon bacillus had become dissociated into a branching form.

Here there is always the question of contaminants. If one considers how these dissociants are detected, one knows that the cultures must be carried along perhaps for years, and therefrom arises the question of contaminants. Dr. Mellon has certainly covered the point of contamination by putting up the proper safeguards. I recall his cogent explanation of why mutation in bacteria had been so slow in gaining recognition—namely, that bacteriologists overlooked or disregarded the mutants. They acted like technicians when new and strange faces crept into their subcultures and glossed over the phenomena on the basis of contaminants. This is a valuable contribution to the study of noncaseating tuberculosis.

DR. MARION B. SULZBERGER, New York: I think Dr. Weidman has done well to emphasize the necessity for careful study and further confirmatory experiments before the drawing of conclusions, and I agree with Dr. Weidman that the lesions here illustrated are perhaps best classified as Boeck's sarcoid, both of the skin and of the lungs. As is well known, the recovery of the tubercle bacillus in this disease is usually difficult, if not impossible. Furthermore, patients often fail to react to tuberculin even in high concentrations. The divergence of this form of noncaseating epithelioid tuberculosis from the usual forms is probably due to the increased or altered resistance to the tubercle bacillus. The explanation of the authors' observations may be that the original usual forms of bacilli themselves become altered by the action of these immunologic forces. This explanation is borne out by previous observations, an early one being that of Jadassohn (Jadassohn, J.: Ueber tuberculoide Veränderungen in der Haut bei nicht tuberöser Lepra, *Arch. f. Dermat. u. Syph.* **47**:429, 1899) in leprosy. Leprosy can present a histologic and clinical picture similar to sarcoid tuberculosis. In a case of sarcoid leprosy Jadassohn searched for a long time before finding any bacilli, and it was only after examination of many sections that he ultimately found some bacilli, which were much altered in size and staining qualities but were nevertheless lepra bacilli. A further verification of the alteration of micro-organisms under immunologic influences was that of Werner Jadassohn (Jadassohn, W.: Die Inokulationstuberkulose der Rellenhaut, *Arch. f. Dermat u. Syph.* **167**:169, 1932), who, working with tubercle bacilli in rats, demonstrated the high degree of resistance to infection, the morphologic alteration of the injected bacilli and the presence of anticutins or tuberculin-neutralizing antibodies in the blood serum. These experiments showed that in the rat there exists a natural state of resistance

to tuberculosis analogous to the acquired stage found in human beings with sarcoid. In the rat there is early development of the histologic picture of sarcoid, a picture almost identical with that which appears in Boeck's cases in human beings.

I should like to suggest to Drs. Beinhauer and Mellon that in these cases the first infection may have been with the ordinary tubercle bacillus and that the dissociation and the various changes of the bacillus may occur in the host and may be due to the immunizing processes of the host acting on and changing the ordinary bacillus to other, morphologically different and less virulent forms.

DR. LAWRENCE G. BEINHAUER, Pittsburgh: I wish to thank the discussers. We mentioned in a previous paper, to which we referred in the report, that the impression given by these lesions was that of sarcoid. We hesitated to attach the name sarcoid to the lesion in this case, because when we saw it it had the appearance of anything but sarcoid, although the histologic picture was the same. This condition is usually found in Negroes. We have observed five cases of this type in which we have been able to recover these dissociants. As mentioned, these patients have an anergy to conventional tuberculin. It is a singular fact how frequently one can use old tuberculin in these cases and get no reaction. With critical R tuberculin the reaction is positive in this and analogous cases. This tuberculin differs in no way from Koch's tuberculin except that it is made from the critical R bacillus, which is morphologically and culturally the same as Koch's bacillus but is not capable of producing progressive tuberculosis.

CRYPTOCOCCUS HISTOLYTICUS ISOLATED FROM SUBCUTANEOUS TUMOR

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A systematic study of a yeast identified as Cryptococcus histolyticus is reported here, in order to help clarify the confusion that now exists in the literature on pathogenic yeasts. Many of the reports have merely described the isolation of a yeastlike organism. Only a few have mentioned any of the characteristics of the isolated organism that might aid in a better classification of those organisms associated with disease processes.

The organism isolated in the case of cutaneous torulosis which I report here conforms to the morphologic and physiologic characteristics of C. histolyticus. As Mook and Moore [1] have recently pointed out, there is much discussion as to the correctness of the terms Torula and Cryptococcus in reference to the etiologic agent of torulosis. The term Torula is commonly used in the literature and has supplanted the correct term, Cryptococcus. Mook and Moore [1] have shown that Cryptococcus is the correct generic name for the organism and should be used in all cases in preference to Torula.

Torulosis as a clinical entity was for many years believed to be confined to the internal organs, especially the brain and the spinal cord. Stoddard and Cutler [2] have emphasized the absence of any cutaneous lesion in their extensive monograph on torula infections. Weidman [3] has reviewed five reported cases of cutaneous torulosis, and Wile [4] has recently added one more case to that list.

REPORT OF A CASE

A Negress 22 years of age was admitted to the university hospital on Jan. 4, 1937, complaining of a swelling on the right wall of the chest, just below the shoulder blade, accompanied with slight irregular fever, weakness and loss of weight. Five weeks before admission the patient had had intermittent sharp pains

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From the Department of Bacteriology and Public Health, University of Georgia School of Medicine.

1. Mook, W. H., and Moore, M.: Cutaneous Torulosis, Arch. Dermat. & Syph. **33**:951 (June) 1936.

2. Stoddard, J. L., and Cutler, E. C.: Torula Infection in Man, Monograph 6, Rockefeller Institute for Medical Research, 1916, p. 1.

3. Weidman, F. D.: Cutaneous Torulosis, South. M. J. **26**:851, 1933.

4. Wile, U. J.: Cutaneous Torulosis, Arch. Dermat. & Syph. **31**:58 (Jan.) 1935.

over the right thoracic region followed by the formation of a hard mass. Pain and growth of the mass continued for three or four weeks before the pain lessened and the growth of the mass apparently ceased.

On examination a tumor about 4 cm. in diameter was found attached to the tenth rib on the right side, just below the angle of the scapula. The tumor was firm and well fixed but not tender. A roentgenogram showed erosion of the tenth rib in the region of the growth. The tumor gave the impression of sarcoma.

On biopsy, an excapsulated mass 3 cm. in diameter was observed, which contained several cubic centimeters of a gummy, blood-stained exudate. Direct smears of the exudate were stained by Wright's stain for blood, and on examination large numbers of yeastlike cells were seen, particularly in the cytoplasm of the giant cells. Some of these intracellular organisms were budding. Water mounts of the exudate revealed numerous round cells with double-contoured highly refractile membranes. Sections of tissue showed many yeastlike organisms in the granulation tissue, with a few giant cells containing the organisms. The Wassermann and Kahn tests were negative. When some of the exudate was planted on Sabouraud's medium, a pure culture of yeast was obtained after the plate had been incubated at 37 C. for forty-eight hours. The spinal fluid was clear and showed no organisms on direct examination of the centrifugated specimen, and no organisms developed when a sample of the sediment was cultured on Sabouraud's medium.

The patient was placed on a diet and given roentgen treatment and potassium iodide. After six weeks the wound had completely healed, and the temperature was again normal. The patient was dismissed and instructed to report monthly for further examinations. After six months she had had no recurrence of the infection and appeared well, except for a continued loss of weight.

MORPHOLOGIC CHARACTERISTICS OF ORGANISM

In the lesions, some of the organisms were apparently encapsulated, rounded and budding and possessed a double-contoured membrane. The cells were usually from 5 to 8 microns in diameter. In cultures the cells varied considerably in size but were always rounded. In old cultures some of the organisms grew as large as 15 microns in diameter. The walls of the larger cells were highly refractive. An actively growing culture showed many budding forms. The buds usually had thinner walls than those of the parent cell. There was never more than one bud on any one cell. Surrounding some of the larger cells, a capsular area several times the width of the cell wall was demonstrated by an india ink preparation, as suggested by Weidman.[3] Many granules were within the older cells as well as some of the young buds, and these granules could be demonstrated beautifully by preparing a wet mount with a dilute solution of methylthionine chloride U. S. P. (methylene blue). Some of these granules were fatlike substances, as shown by staining with sudan III. No mycelium was produced, nor was there evidence of endosporulation, even after the organisms had been cultured and subcultured for six months. These morphologic characteristics conform to the picture of cryptococci as described by Benham.[5] The colo-

5. Benham, R. W.: The Fungi of Blastomycosis and Coccidioidal Granuloma. Arch. Dermat. & Syph. **30**:385 (Sept.) 1934.

nies produced on Sabouraud's medium were smooth, moist, raised and mucoid. The colonies growing on plates incubated at room temperature were white at first and on continued incubation turned creamish and grew to 8 mm. in diameter.

CULTURAL CHARACTERISTICS OF ORGANISM

The organism isolated on Sabouraud's medium grew well when subcultured on most bacteriologic mediums. The yeast, however, grew best at room temperature. No pellicle was produced in broth cultures, and the medium was usually clear above the sedimented growth. Indole was not produced. Starch was not hydrolized. Gas was not produced in any of the sugar broths inoculated. The table shows the results obtained when various carbohydrates were inoculated with the organism. These results indicated that after the organism had been repeatedly subcultured, its fermentative ability was increased. These results show also that if fermentation does occur it occurs slowly and in some carbohydrates only after prolonged incubation. Most writers in reporting the results of carbohydrate fermentation with yeastlike organisms have failed to state how long the cultures were incubated. The table shows the importance of holding the subcultures for at least thirty days before recording the reaction.

	Carbohydrates							
Organism Inoculated	Dextrose	Lactose	Sucrose	Maltose	Mannitol	Xylose	Dextrin	Inulin
C. histolyticus one week after isolation	A-14	0	A-15	A-40	0	0	0	0
C. histolyticus five months after isolation	A-5	0	A-8	A-15	0	A-23	A-23	0

A indicates acid; 0, no reaction. The numeral indicates the number of days' incubation at room temperature before acid occurred.

IMMUNOLOGIC REACTIONS

A vaccine was prepared by suspending several loopfuls of cells in a solution of sodium chloride, so that a turbidity was produced to represent a billion organisms per cubic centimeter. This was then tested for sterility. When 0.1 cc. of this vaccine was inoculated intracutaneously into the patient's forearm an erythematous area about 2 cm. in diameter developed in twenty-four hours. No reactions occurred when the vaccine was tested on controls. The erythematous area on the patient's arm gradually disappeared after twenty-four hours.

Complement fixation tests were made, because Martin [6] had reported success with that method in his cases of blastomycosis. Such tests, how-

6. Martin, D. S.: Complement-Fixation in Blastomycosis, J. Infect. Dis. **57**: 291, 1935.

ever, gave negative results repeatedly in the case of cutaneous torulosis reported in this paper.

PATHOGENICITY FOR LOWER ANIMALS

The organism was found to be avirulent for rabbits, guinea-pigs, white rats and white mice when inoculated intraperitoneally. However, the organism could be recovered from the spleens of mice ten days after an intraperitoneal inoculation. When rabbits were inoculated intracutaneously with 0.1 cc. of a broth culture of the yeast, an erythematous area appeared within forty-eight hours and progressed to form a subcutaneous abscess. The area would become necrotic and rupture, with a creamy, thick exudate before healing.

Two rabbits were inoculated intravenously and two more intratesticularly, with 0.5 cc. of a broth culture of C. histolyticus. All four animals remained well. Thirty days later an area was shaved on the side of each of these rabbits, and intracutaneous tests were made with 0.1 cc. of a killed culture of C. histolyticus; control tests were made with similarly prepared killed cultures of Saccharomyces cereviseae and Haemophilus ducreyi. The results in controls were all negative, whereas an erythematous area from 6 to 12 mm. in diameter developed in forty-eight hours in the animals previously inoculated with 0.1 cc. of the specific vaccine. The erythematous area persisted for from five to seven days. Six normal rabbits gave no reaction when inoculated with 0.1 cc. of the killed culture of C. histolyticus. These six control rabbits gave no reaction when the cutaneous test was repeated on them thirty days later. The four rabbits inoculated with the live culture of C. histolyticus gave negative reactions to the complement fixation test at the time they were sensitive to the specific cutaneous test. These rabbits were still sensitive to the specific cutaneous test four months after the original inoculation.

SUMMARY

A case of cutaneous torulosis is reported in which Cryptococcus histolyticus was isolated.

Morphologic and cultural characteristics of this organism are recorded. Particular emphasis is placed on the importance of holding subcultures of sugar broths for thirty days or more before recording the reaction.

Cryptococcus histolyticus isolated from this patient proved to be avirulent for small laboratory animals. Subcutaneous abscesses could be produced regularly in rabbits. Intracutaneous tests made on rabbits inoculated thirty days previously with a live culture of C. histolyticus were positive within forty-eight hours.

PARAPSORIASIS EN PLAQUES DISSÉMINÉES AND INCIPIENT MYCOSIS FUNGOIDES

A CRITICAL REVIEW WITH A REPORT OF AN ILLUSTRATIVE CASE

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At present the widest diversity of opinion exists in relation to the classification and differential diagnosis of parapsoriasis in patches. In 1910 Arndt,[1] after an exhaustive study of the subject, suggested the title Brocq's disease to indicate that the condition was an independent entity. It is now customary to subdivide parapsoriasis into three or four types, but in late years the relation of the several varieties has been more or less questioned by a number of authorities. For example, Civatte [2] has only recently (1936) stated, "The clinical unity of parapsoriasis appears, therefore, after a lapse of thirty years, to be more disputable than at the time when the group was first created." This statement seems the more significant because this observer wrote his celebrated thesis [3] (1906) under the tutelage of Brocq. Most authorities who question the essential unity of the conditions embraced within the category of parapsoriasis seem not to be convinced that similarities in histologic picture, if they exist,[2] are sufficiently distinctive to warrant assumption of a close relation, particularly since the minute anatomic features possess few, if any, distinguishing characteristics; nor are they satisfied that clinical *faits de passage*, as claimed by Brocq, occur frequently enough to justify belief in the unity of the several variants of the disease. When instances of such transition have been recorded, such authors as Juliusberg [4] have regarded their importance as lessened by virtue of their rarity, while others, such as Kissmeyer,[5] have sug-

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1. Arndt, G.: Ueber Brocqsche Krankheit (érythrodermie pityriasique en plaques disséminées) nebst einigen Bemerkungen zur Frage der Parapsoriasis, Arch. f. Dermat. u. Syph. **100**:7, 1910.

2. Civatte, A.: Le parapsoriasis, in Darier, J.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 7, p. 686.

3. Civatte, A.: Le parapsoriasis de Brocq, Thèse de Paris, no. 216, 1906.

4. Juliusberg, F.: Die Brocqsche Krankheit, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol: 7, pt. 1, p. 326.

5. Kissmeyer, A.: La maladie de Brocq (érythrodermie pityriasique en plaques disséminées), Ann. de dermat. et syph. **6**:378, 1925.

gested other interpretations of the morphologic attributes. The debate has, therefore, for the most part revolved about the status of parapsoriasis en plaques.

In the transactions of dermatologic societies there have been many reports of cases of parapsoriasis in patches, but in few instances has the diagnosis received unqualified acceptance. Yet it is in large measure on the basis of such descriptions that eclectic accounts of this disorder have been given, and it seems worth while to review the available data and, if possible, to sift fact from impression. The records of society transactions have proved to have immense value because of the occasional comments regarding the subsequent course of the disease in patients whose condition was originally diagnosed as *érythrodermie pityriasique en plaques disséminées* (Brocq[6]). In the background in all accounts of parapsoriasis in patches has been the disturbing question of incipient mycosis fungoides; indeed, there is hardly a case reported by one observer as an instance of the former condition that has not at one time or another been classified by other observers as an example of the latter.

This report has for its basis the study of an unusual case in which Brocq's disease some eight years after onset became transformed into typical mycosis fungoides, exhibiting infiltrated bizarre plaques and tumors. On the foundation of a considerable experience, Civatte[7] in 1930 denied the possibility of conversion of the one malady into the other, though in several previous communications he had emphasized the caution required in differential diagnosis between the two conditions; according to his most recent publication (1936), however, he has apparently come to regard the possibility of such metamorphosis with more favor. This sequence of disorders has been recorded several times, but the real incidence of the association appears to have escaped notice in reports by Gougerot, Meyer and Eliascheff,[8] Gougerot and Burnier,[9] Milian and Lereboullet,[10] Wise and Rosen,[11] Sherwell,[12]

6. Brocq, L.: Les érythrodermies pityriasiques en plaques disséminées, Rev. gén. de clin. et de thérap. **11**:577, 1897.

7. Civatte, A., in discussion on Milian and Lereboullet.[10]

8. Gougerot, H.; Meyer, J., and Eliascheff, O.: Parapsoriasis et mycosis fungoide, Arch. dermat.-syph. de la clin. Hôp. St. Louis **8**:107, 1936.

9. Gougerot, H., and Burnier: Parapsoriasis en plaques avec poïkilodermie: Transformation ultérieure en mycosis fungoïde, Bull. Soc. franç. de dermat. et syph. **41**:1528, 1934.

10. Milian, G., and Lereboullet: Érythrodermie pityriasique en plaques et mycosis fungoïde, Bull. Soc. franç. de dermat. et syph. **37**:1292, 1930.

11. Wise, F., and Rosen, I.: A Case of Early Mycosis Fungoides Clinically Indistinguishable from Parapsoriasis of Brocq, J. Cutan. Dis. **34**:95, 1916.

12. Sherwell, S.: Case of Parakeratosis Variegata (Unna), Lichen Variegatus (Crocker), or Érythrodermie Pityriasique en Plaques Disséminées (Brocq), J. Cutan. Dis. **21**:514, 1903; cited by Ormsby.[22]

Hyde,[13] Veiel,[14] Lutz[15] and Rosen,[16] among others. The list becomes even more imposing when one adds instances of parakeratosis variegata and retiform parapsoriasis (the relation of these types to the en plaque form being variously considered) that have terminated in mycosis fungoides (Jamieson,[17] Unna, Santi and Pollitzer,[18] Hudelo and Gastou[19] and Civatte[20] among others). It will be seen that in practically all these examples parapsoriasis was not simply confounded with incipient mycosis fungoides, but the original dermatosis conformed to the postulates laid down by Brocq for the recognition of parapsoriasis. Contrariwise, many eruptions have been accepted as examples of Brocq's disease, though they revealed striking, and in some cases fundamental, deviations from classic criteria. In comparison with cases of the en plaque variety that appear to be authentic because of observations conducted over many years (such as those reported by Wise[21] and Ormsby[22]), this incidence of complicating mycosis fungoides will seem noteworthy. The problem is, moreover, rendered more intricate by the opinions of other observers relative to cases frequently cited as typical examples of parapsoriasis in patches, many of these having been regarded as instances of prefungoid mycosis (fungoides), such as

13. Hyde, J. N., in discussion on Ravogli.[37]

14. Veiel, T., in discussion on Pollitzer.[21b]

15. Lutz, W.: Case Originally Diagnosed as Parapsoriasis; Finally, Regarded as Premycotic Erythrodermia, Schweiz. med. Wchnschr. **6**:351, 1925.

16. (*a*) Rosen, I.: Parapsoriasis en Plaques, Arch. Dermat. & Syph. **30**: 597 (Oct.) 1934. (*b*) Abramowitz, E. W.: Early Stage of Mycosis Fungoides, ibid. **36**:200 (July) 1937. (Same case as that reported by Rosen.[16a]). The pathologic report on the first biopsy specimen was "retrogressing parapsoriasis" and on the second, chronic eczema; the last specimen revealed the probable changes of early mycosis fungoides.

17. Jamieson, W. A., cited by Fox, T. C., and MacLeod, J. M. H.: On a Case of Parakeratosis Variegata, Brit. J. Dermat. **13**:319, 1901.

18. Unna, P. G.; Santi, and Pollitzer, S.: Ueber die Parakeratosen im allgemeinen und eine neue Form derselben (Parakeratosis variegata), Monatsh. f. prakt. Dermat. **10**:404, 1890. The case or cases in this paper are discussed further by Brocq[6] and Pollitzer.[31]

19. Hudelo and Gastou: Cas probable de parakeratosis variegata, Ann. de dermat. et syph. **5**:1090, 1904.

20. Civatte, A., in discussion on Gaté, M. M., and Michel, P.: A propos d'un cas de poïkilodermie, Bull. Soc. franç. de dermat. et syph. **36**:848, 1929; footnote 3.

21. (*a*) Wise, F., in discussion on Rosen,[16a] p. 598. (*b*) Pollitzer, S.: Érythrodermie Pityriasique en Plaques Disséminées, J. Cutan. Dis. **29**:558, 1911; cited by Wise.[21a]

22. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin, ed. 4, Philadelphia, Lea & Febiger, 1934, p. 904.

Crocker's [23] xantho-erythroderma perstans and White's [24] case 2 by Civatte,[3] Anthony's [25] case by Pernet [26] and numerous other examples recorded in transactions of societies. Furthermore, there have been additional instances in which the possibility of incipient mycosis fungoides was eliminated on the basis of criteria subject to criticism—the cases of Dubreuilh and Méneau [27] and Pillon,[28] for instance.

Analysis of data collated from the literature reveals that this differential diagnosis cannot be established with certainty by the use of criteria hitherto considered decisive. The final diagnosis of parapsoriasis in patches in isolated cases observed over many years by Wise and by Ormsby must be considered in the light of the important example of the disease which was described with admirable thoroughness by Gougerot and Burnier,[9] in which mycosis fungoides supervened only after some twenty-two years. It will be of great interest to trace the origin of the conception of parapsoriasis in patches, noting the manner in which it arose and was accepted, though a large proportion of the original cases turned out, according to information gleaned from recorded discussions, to be examples of mycosis fungoides. Hence it becomes pertinent to inquire:

1. Is the relation of parapsoriasis in patches to incipient mycosis fungoides a closer one than has hitherto been assumed? (a) Are the clinical criteria for differential diagnosis between the two disorders entirely satisfactory? (b) Can the two conditions be distinguished with certainty on the basis of histologic study alone; in other words, do the anatomic alterations constitute the ultimate criterion in all cases? (c) Is the prognosis in the average case in which a diagnosis of parapsoriasis en plaques has been made as innocuous as one is commonly led to believe?

2. Are there cases in which incipient mycosis fungoides fails to satisfy the ordinary clinical and pathologic criteria for its recognition? (a) When the condition in such cases resembles parapsoriasis en plaques, can it always be differentiated from Brocq's disease? (b) Does the finding of "banal" histologic alterations eliminate the diagnosis of mycosis

23. Crocker, H. Radcliffe: Xantho-Erythroderma Perstans, Brit. J. Dermat. **17**:119, 1905.

24. White, C. J.: Case of Brocq's Érythrodermie Pityriasique en Plaques Disséminées, J. Cutan. Dis. **18**:536, 1900.

25. Anthony, H. G.: The Report of a Case of Parakeratosis Variegata, J. Cutan. Dis. **24**:455, 1906.

26. Pernet, G., in discussion on Ravogli.[37]

27. Dubreuilh, W., and Méneau: Un cas de parapsoriasis (Brocq), Ann. de dermat. et syph. **4**:166, 1903.

28. Pillon, M.: Parapsoriasis en plaques, Bull. Soc. franç. de dermat. et syph. **38**:711, 1931.

fungoides with certainty? (c) Does prefungoid mycosis fungoides in all cases develop to the stage of infiltrated plaques and tumors? Are there instances of the disease in the incipient stage in which the cutaneous lesions remain unaltered for many years in a manner simulating the course of parapsoriasis en plaques?

Data collected from various sources provide answers to these fundamental questions.

REPORT OF CASE

On April 11, 1932, J. K., a woman aged 28, was first observed in the dispensary service of Dr. G. M. MacKee. She had had a generalized eruption constantly during the preceding four years, which was apparently refractory to various types of treatment. The onset was not associated with marked itching; pruritus at the most was mild, inconstant and infrequent, a point recently confirmed by the patient, who is under my care at present. The dermatosis began as brownish blotches on the abdomen and the back. The lesions, according to the patient, who is intelligent, resembled "liver spots." The eruption then spread gradually over the remainder of the body, including the face. When the patient was first observed there was a scaling erythematous, slightly pigmented rash composed of fairly well defined lesions, ranging in size from that of a pea to that of a palm, arranged discretely and in confluent plaques (fig. 1). A history of ingestion of feenamint was elicited, and accordingly suspicion was directed to the possibility that the eruption was of drug origin. On the same day a specimen of skin was taken for biopsy; the pathologic report by Dr. D. L. Satenstein read as follows: "There is a superficial exudative inflammatory process in the subpapillary zone. No pigment is present. The changes are insufficient for a diagnosis of parapsoriasis. The picture may fit in with a stationary drug eruption."

On Feb. 11, 1933, there were numerous pale erythematous areas varying in size from that of a pea to that of a palm scattered over the entire body. The individual lesions were relatively sharply defined and slightly infiltrated (?). There was fine furfuraceous nonadherent scaling over all the patches. Some of the lesions, especially those on the back of the neck, were somewhat "lichenified," as indicated by some exaggeration of cutaneous markings. There was a definite tendency to symmetrical distribution, notably on the face, where the configuration was of the bat-wing type. Of late there had been some pruritus, confirmed by scratch marks on the extremities. There was some alopecia on a few patches, especially those located on the forearms, but there was no evidence of atrophic changes. The general health was unimpaired. Since the previous biopsy had been made, phenolphthalein preparations had been assiduously avoided. Several large patches on the neck and on the back contained within them islands of normal skin. Another specimen of skin was removed from the left side of the back for histologic examination, and the report by Dr. D. L. Satenstein indicated chronic neurodermatitis or a drug eruption. It was felt, however, that the application of iodine to the lesion might have modified the minute anatomic features significantly; accordingly, nine days later, a third specimen of skin was taken from the edge of the same lesion, for additional study. This time Dr. Satenstein's report read: "There is a superficial exudative inflammatory process of no special character. A diagnosis is not possible." In the meantime, patch tests were performed with about a dozen suspected common irritants, ranging from pyrethrum to Evening in Paris perfume, all with negative results. During one month the patient received eight ultraviolet irradiations to the entire trunk with a quartz mercury vapor glow

lamp and three exposures at weekly intervals to each side of the face of ¼ skin unit (75r) of unfiltered roentgen radiation. These therapeutic procedures were unavailing. The final diagnosis was drug eruption or neurodermatitis, based on one of the histologic reports, though the consensus of the dermatologists consulted was that the condition belonged in the group of parapsoriasis en plaques. The

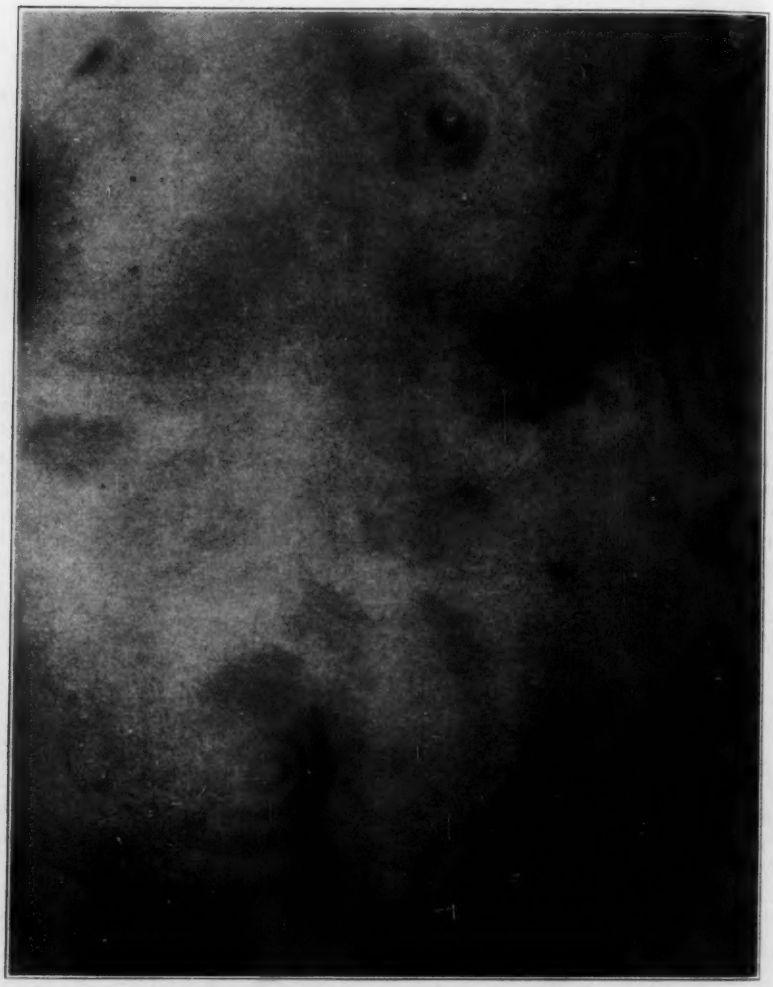

Fig. 1.—Superficial, nonelevated brownish red patches on the back and on the buttocks, exhibiting the clinical features of parapsoriasis in patches. The extent of the eruption some four years after onset is shown.

latter view was subsequently concurred in by other dermatologists whom the patient consulted.

Between 1933 and early 1936 she was observed by several internists. The only physical abnormality, marked overweight, and the history of irregular menstrua-

tion and oligomenorrhea suggested the possibility of mild insufficiency of the pituitary gland, though there were no other evidences of endocrine stigmatization. She was therefore treated with pituitary extract and placed on a high protein reducing diet. These measures were unavailing.

On Jan. 11, 1936, the patient was first seen by me. The clinical picture was at that time typical of mycosis fungoides in the infiltrated plaque and tumor stage. Only in the past several months had the lesions become elevated, and for the first time the patient experienced paroxysms of pruritus, notably at night. Sulfur therapy had been used recently as a local measure, and various types of intravenous medication had been tried, without marked success. The menses were still irregular and scanty. When she was first observed by me, there was disseminated all over the body an eruption composed of various types of lesions, many of them of bizarre shape. On the scalp there was moderate desquamation, several tumors reaching the size of a small bean. The cheeks revealed an erythematous, scaling, slightly thickened, diffuse butterfly-shaped lesion, which encroached on the neighboring parts of the forehead and the chin. On the forehead and encroaching on the right side of the anterior portion of the scalp for a short distance was a curious group of reddish brown nodules arranged in a semicircle. The trunk and the limbs were the sites of reddish brown lesions in discrete and confluent patches of variable dimensions. Some of them showed central irregular areas composed of apparently normal skin. For the most part the plaques were definitely thickened. A few elevated tumor-like areas were encountered on the right arm, the thighs and the upper portion of the chest, with similar smaller lesions scattered over the anterior and posterior portions of the trunk. There were a few slightly enlarged lymph nodes on both sides of the neck along the sternocleidomastoid muscles. The spleen and the liver could not be palpated. Physical examination disclosed no other abnormalities of note, aside from overweight. The general health had not been impaired throughout the illness, the patient being disturbed only because of the unsightliness of the skin and the occasional attacks of pruritus. The diagnosis of mycosis fungoides was therefore postulated. A biopsy specimen was taken from an infiltrated, somewhat raised plaque on the upper portion of the arm, and ½ skin unit (180 r) of unfiltered roentgen radiation was administered to the group of lesions on the right side of the forehead, as a therapeutic and a diagnostic procedure. A blood count showed 16,900 leukocytes. The rectal temperature on several occasions was 99.5 F. The histologic examination confirmed the clinical impression of mycosis fungoides. One week after the lesion on the forehead was irradiated, it had flattened considerably, and within about three weeks complete involution had occurred. The various areas of the body were given roentgen treatments in small doses, and there was remarkable involution of the entire eruption. At one time solution of potassium arsenite, which was being taken in moderate doses, had to be discontinued, as the patient manifested intolerance for it. During the summer of 1936 the patient was practically free from cutaneous lesions for the first time in eight years. The facial lesions which had in 1933 been refractory to roentgen therapy had responded remarkably. The patient has recently returned with a relapse of the cutaneous condition, not as severe, however, as when first observed in 1936. It is interesting to note that during the period of involution of the eruption the menses had become more regular and less scanty.

Additional Laboratory Data.— In August 1933 determinations by Dr. M. A. Goldzieher showed the basal metabolic rate to be + 9, the cholesterol content of the blood 200 mg. and the uric acid content 4.2 mg. per hundred cubic centimeters. On Jan. 14, 1936, the blood count revealed 4,430,000 red blood cells and 16,900 white blood cells, with 78 per cent polymorphonuclear leukocytes.

Biopsies.—A complete account of the anatomic alterations will be given, as such data are of particular importance because of (1) the fact that three specimens of skin were studied, which tends to eliminate the possibility that the specific changes of mycosis fungoides had been overlooked through chance; (2) the light which is thrown on the nature of the "incipient" process in this case, the biopsy specimens having been taken some four years after the onset of an eruption that had remained stationary; (3) the opportunity afforded to secure the opinions of several competent dermatohistopathologists and to compare them with one another in a case of this type.

Fig. 2.—Histologic picture of lesion present for some four years, disclosing no evidence of a process causing clinical infiltration. The epidermal changes were minimal, the principal alterations appearing about the subpapillary and the perifollicular vessels, with a nonspecific inflammatory reaction (see text).

First Biopsy, April 11, 1932: The epidermis seemed slightly thinned but otherwise unaltered. Most of the granular layer was retained. The basal membrane was more hazy than normal. No nests of cells were encountered within the epidermis. The papillary bodies revealed moderate edema. The cellular infiltrate situated principally about some of the subpapillary vessels was not pronounced; it was accompanied by occasional lymphocytes scattered at random in the papillary layer. The subpapillary vessels revealed swollen endothelium and were surrounded

by a zone of edema in which were embedded lymphocytes, cells of the connective tissue series and an occasional mast cell. In areas the outlines of these blood channels were indistinct. In some sections there was a similar cellular reaction about the vessels in relation to a pilosebaceous system, with invasion of the more superficial portions of the sebaceous glands by lymphocytic cells. It was agreed by Drs. J. F. Fraser, E. A. S. Barthel and T. J. Riordan that the alterations were nonspecific and that mycosis fungoides could not be diagnosed on the basis of these changes. The last-named observer believed that under ordinary circumstances the diagnosis of parapsoriasis might be justified by a process of exclusion (fig. 2).

Fig. 3.—A second section taken about eight months after the first, showing more pronounced epidermal changes and a nonspecific inflammatory reaction about the subpapillary vessels (see text).

Second Biopsy, Feb. 11, 1933: The histologic alterations were the same as those seen in the previous slides except that (1) there was moderate proliferation of the rete pegs, accompanied with slight intercellular edema of the spinous layer and the presence of a few wandering lymphocytes, and (2) the cellular infiltration was somewhat more pronounced, though similar and with the same distribution about the subpapillary vessels. Most observers regarded these changes as consistent with the picture of an ordinary chronic nonspecific inflammatory process (fig. 3).

Third Biopsy, Feb. 20, 1933: The histologic picture was similar to that presented by the other specimens. In one area in the lower part of the epidermis there was a multilocular vesicle (iodine effect?). The slide was considered by all observers to show a chronic exudative inflammatory process.

Fourth Biopsy, Jan. 14, 1936: The epidermis was irregularly and markedly acanthotic. There was some intercellular edema, and the intercellular bridges of the spinous layer were more conspicuous. Parakeratosis was present in scattered areas. Throughout the upper part of the cutis and in large masses situated in the

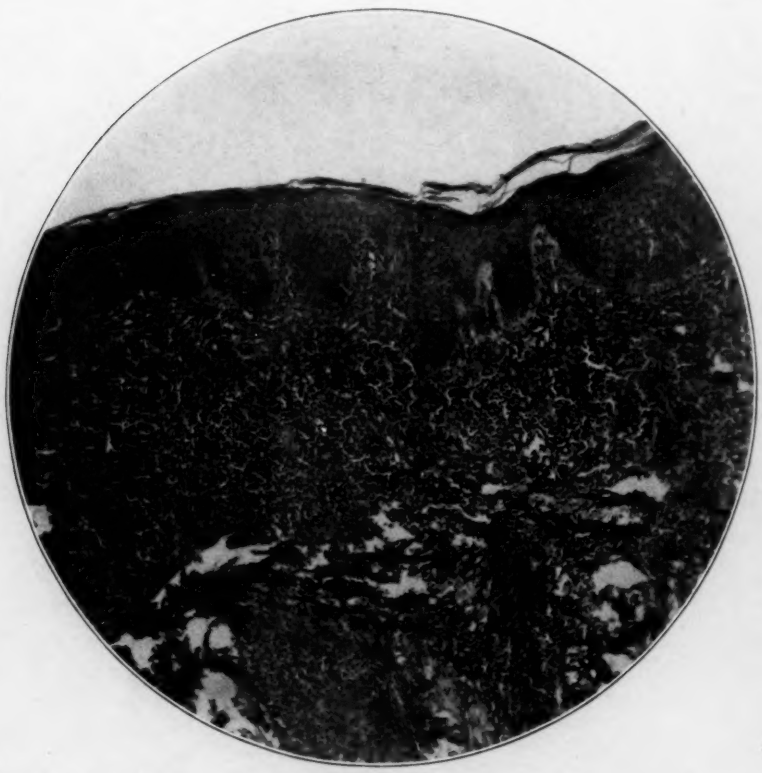

Fig. 4.—Section taken about four years after the first, or some eight years after the onset of the dermatosis, showing marked epidermal proliferation with an intense cellular reaction in the upper third of the cutis, the lower limit being sharply defined in many areas. Cellular infiltration is present in the deeper portions of the cutis in circumscribed foci (see text).

middle and lower parts was an intense cellular infiltration composed chiefly of many large cells (epithelioid cells and wandering connective tissue or reticular cells) and smaller lymphocytic cells, with scattered polymorphonuclear leukocytes and rare plasma cells and eosinophils. There were occasional large structures containing several oval pale-staining nuclei; these might have been blood vessels cut tangentially. Coursing through the cellular masses were blood channels exhibiting swollen endothelial cells. There were a fine and a coarse "reticulum" inter-

spersed with the infiltration. The circumscribed character of the cellular masses was seen especially well in the upper portion of the cutis. Mitotic figures were not seen.

Drs. J. F. Fraser and D. L. Satenstein were of the opinion that the alterations were those of mycosis fungoides; Drs. A. E. Barthel and T. J. Riordan classified the changes as lymphoblastoma (figs. 4 and 5).

Comment.—When the eruption was observed in 1932, some four years after onset, it presented clinical attributes fulfilling the criteria postulated by Brocq for the diagnosis of *érythrodermie pityriasique en plaques disséminées.* The dermatosis was composed of brownish red discrete and confluent plaques, which definitely favored the trunk; the morphologic features had been fairly constant;

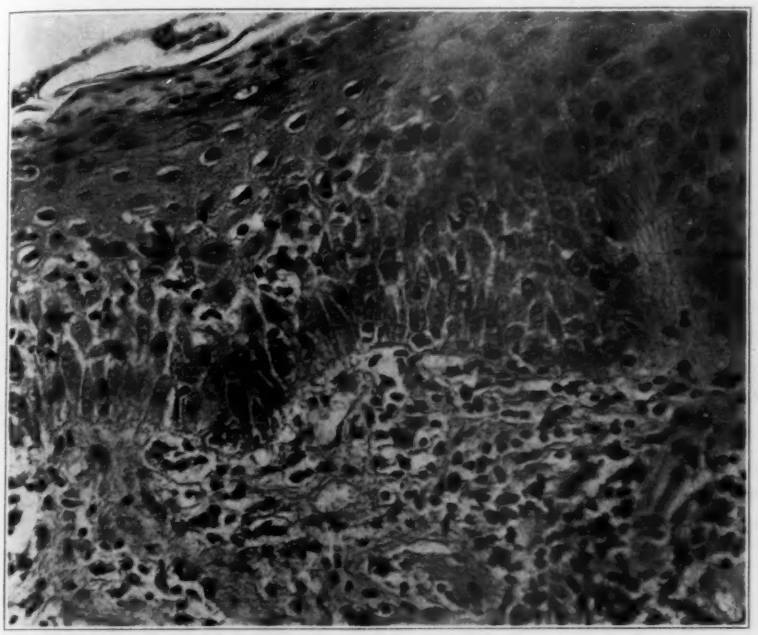

Fig. 5.—High magnification of a portion of the section shown in figure 4. The nature of the epidermal changes and the character of the infiltration are depicted (see text).

the lesions had been refractory to many varieties of treatment, and pruritus had been mild and inconsequential. The patches were covered by a fine furfuraceous scale and revealed what might be interpreted as superficial "lichenification," a phenomenon commonly encountered in dermatoses labeled parapsoriasis en plaque (Arndt, Civatte). The general health was unimpaired.

Histologic examination confirmed the clinical impression that the process was superficial, the minute anatomic alterations furnishing little basis for a belief that the original eruption was infiltrated, as the cellular collections in the cutis were relatively insignificant in extent and distribution; edema was moderate and epithelial proliferation was relatively mild. Infiltration of bandlike masses of cells, such as that seen in mycosis fungoides and other diseases, was therefore absent, even four years after the onset of the dermatosis. It will be seen from

examination of the histologic picture that the process appeared to have its origin at the level of the subpapillary vessels and directly about them. If one concedes that the condition belonged in the category of mycosis fungoides from its inception, though the banality of the microscopic alterations did not permit recognition of the disease ab initio, there seems to be evidence substantiating the view of Huie [29] that mycosis fungoides commences about the subpapillary vessels and then spreads upward and downward.

The failure of the facial lesions to respond to roentgen therapy early in the course of the disorder seems interesting and may possibly be attributable to the few treatments administered at that time or to the lack of the characteristic radiosensitive infiltration of mycosis fungoides. In 1936 the patients still presented the same butterfly-shaped eruption on the face, with lesions showing only slight infiltration clinically; yet the response to radiation was prompt at that time. It is possible that on the later occasion histologic examination would have disclosed more definite evidence of specific cellular reaction.

It will be of interest now (1) to review and to analyze the original contributions on which the conception of parapsoriasis in patches was built and (2) to discuss the differential diagnosis between this disorder and incipient mycosis fungoides.

ORIGIN OF THE CONCEPTION OF PARAPSORIASIS EN PLAQUES

The concept of parapsoriasis in patches and its congeners was gradually built up in twenty years on the basis of the original observations reported, in chronologic order, by Unna, Santi and Pollitzer, Brocq, White, Crocker, Civatte and Arndt, among others. Without denying the authenticity of reports of this condition, it seems interesting to analyze them on the basis of the relation between parapsoriasis in patches and incipient mycosis fungoides, as many important points are involved. It will be my principal purpose to bring together data relative to the eventual outcome in many of the cases and to show how opinions have fluctuated over periods of years, especially in regard to fundamental ideas.

In 1890 Unna, Santi and Pollitzer [18] described two instances of so-called parakeratosis variegata. Seven years later (1897) Brocq [6] saw one of their patients in Paris and noted that the eruption was more psoriasiform than that presented by the subject of his original report on *érythrodermie pityriasique en plaques disséminées.* Another seven years elapsed (1904) before Brocq [30] accidentally mentioned that infiltrated plaques of mycosis fungoides had now developed in Unna's case and that in several other instances parakeratosis variegata had terminated similarly. In 1898 Jamieson [17] demonstrated three unusual examples of what was considered anomalous lichen planus by him and McCall

29. Huie, cited by Sequeira, J. H.: Discussion on Mycosis Fungoides, Brit. J. Dermat. **26**:216, 1914.

30. Brocq, L., in discussion of Hudelo and Gastou.[19]

Anderson, probable "premycosis" by Morris and Crocker, and undoubted parakeratosis variegata by Unna. Of these three patients only one could be followed, and of him Jamieson wrote (1901): "The worst case was for a time in my ward and he developed tumours like those of Mycosis Fungoides on his face and body. . . ." In 1934 Pollitzer,[31] discussed the case of so-called parapsoriasis en plaques presented by Rosen [16a] and subsequently shown with reasonable histologic certainty to be mycosis fungoides (Abramowitz [16b]). He mentioned that in one of the two cases reported jointly with Unna and Santi mycosis fungoides had developed. This case may possibly have been the same as that mentioned by Brocq,[32] probably case 1 of their report (involving an eruption that had remained unaltered for four years or more and was not accompanied by subjective symptoms).

In 1897 Brocq [6] introduced the name *érythrodermie pityriasique en plaques disséminées* to designate the condition in a single case reported by him, but throughout his memorable communication the delicate question of premycotic eruption loomed large. Thus, he stated:

> The red, dry, desquamating eruption appearing in the beginning in certain cases of mycosis constitutes the veritable stumbling block for the morbid type that we are attempting to establish. In reality, nothing can demonstrate in an absolutely peremptory manner, in spite of the recent progress of histology, whether we are or are not in the presence of the larval stage of mycosis. For fourteen years we have been able to follow a young woman who presented here and there over the entire body red scaly patches rather analogous in aspect to that which you note in the subject that we are studying, and it has been only at the end of this time that we have seen formed in her the first mycotic infiltration. But her eruption was eminently pruritic; the plaques were of more intense red hue; in their intervals one found small elements quite analogous to small papules, and the general aspect of the dermatosis was much more mottled than that in the case that we have now under our eyes.

The differential points used, therefore, to establish a new clinical entity were the general aspect of the patient, the paleness of the lesions, the type of scaling and, above all, the almost complete absence of pruritus. In support of his thesis, Brocq saw analogies to Unna's cases, one at least of which later turned out to be an instance of mycosis fungoides. No particular significance was attached to the history of general pruritus commencing about two years before the appearance of cutaneous lesions and its disappearance when the lesions appeared. In concluding his paper Brocq recognized a variety of para-

31. Pollitzer, S., in discussion on Rosen,[16a] p. 598.

32. In a personal communication dated Feb. 10, 1937, Dr. Pollitzer stated that he did not know whether the case mentioned by him [31] was the same as the one to which Brocq referred [30]; it was stated in the same letter that the pathologic alterations in the cases reported by Unna, Santi and Pollitzer were not those of mycosis fungoides at the time of the original report in 1890.[18]

psoriasis associated with severe itching and having clinical attributes making it difficult to differentiate from the premycotic eruptions, and he said it was necessary, perhaps, to classify the condition in the latter category. In 1902 Brocq [33] in a complete review of the subject reported two additional cases; his third example was interesting because it was presented as an instance of nonscaly parapsoriasis en plaques in which several patches showed clear centers, resulting in a circinate configuration, and there was moderate pruritus. These instances were observed for only short periods. In addition, two more examples were given by Brocq as illustrating *faits de passage* in relation to the other varieties of parapsoriasis, but it seems fair to note that Jadassohn [34] (1906) and others have denied the importance of his reports in this connection. In 1904 Brocq,[30] having given the valuable information on parakeratosis variegata already cited, conceded, on the basis of the histologic picture described tentatively by Darier, that the case presented by Hudelo and Gastou was possibly one of incipient mycosis fungoides. In 1921 Brocq [35] wrote as follows in his celebrated textbook:

> There are cases of mycosis fungoides which, during long periods in the beginning, assume the objective aspects of early parapsoriasis en plaques. On clinical examination it is absolutely impossible to differentiate these two affections. We must lay down as a practical rule that one must be suspicious of a beginning of mycosis fungoides every time cutaneous lesions resembling parapsoriasis en plaques are accompanied by pruritus or present in areas a certain degree of dermic infiltration. It is necessary in these cases to do minute histologic studies in order to ferret out premycosis.

It will be shown, however, that this last sine qua non for diagnosis does not furnish an absolute criterion for differentiation of the two disorders.

When in 1900 White [24] recorded three instances of parapsoriasis in patches, he noted analogies between his cases and the one recorded by Brocq three years before, but, unlike the latter observer, he could not see any resemblances to Unna's parakeratosis variegata. It is noteworthy that in his first patient the face and neck were involved, while the second patient complained of some pruritus. In discussing the differential diagnosis White stated:

> I am aware that the erythematous stage of mycosis fungoides has been observed to precede by more than 12 years the development of its other features and that this condition is sometimes almost the exclusive manifestation up to the fatal termination of the case. Yet in the cases I have observed the lesions of this stage

33. Brocq, L.: Les parapsoriasis, Ann. de dermat. et syph. **3**:433, 1902.

34. Jadassohn, J.: Fall zur Diagnose: Érythrodermie pityriasique en plaques disséminées, Verhandl. d. deutsch. dermat. Gesellsch. **9**:398, 1906.

35. Brocq, L.: Précis-atlas de pratique dermatologique, Paris, Gaston Doin & Cie, 1921.

are *never* of such uniform size or remain so small as those in our patient. The hyperemia is much more decided, and the infiltration more marked. There is, however, *never* the regularity in the occurrence of the cutaneous manifestations as in this case.

Aside from exceptions to the points enumerated in differential diagnosis, I shall have occasion to note the opinion of Civatte on the relation of the condition in White's first two cases to incipient mycosis fungoides.

In 1905 Crocker [23] recorded a series of ten cases of which the first nine resembled one another closely, and at the suggestion of Pernet called the condition xantho-erythroderma perstans. The tenth case was apparently classified as one of mycosis fungoides, even though itching was not a complaint; nine exposures of a patch to roentgen radiation caused its disappearance, though the history of the eruption went back some nine or ten years. In the remaining cases there were many points of interest. One of the patients was seen by Hallopeau, Gastou, Jacquet and Pautrier, who unanimously refused to accept his case as an example of the dermatosis described by Brocq; indeed, Crocker himself had first regarded the case as one of possible incipient mycosis fungoides *faute de mieux*. In this instance the face was involved slightly. In another patient itching was a striking symptom. Peculiar to this group of cases were three outstanding attributes: (1) in nearly all there was distinct infiltration in a large proportion of the lesions; (2) many patches exceeded in size the limits described by Brocq; (3) disappearance of the eruption occurred in several instances. Of note was the fifth case, in which the patient had observed a small patch on the calf about thirty years before, though the principal eruption was more recent. What the eventual outcome of these cases was no one knows; it is, however, certain that Civatte [3] in the following year refused credence to the diagnosis, placing the cases rather among those of incipient mycosis fungoides. Of fundamental interest in this connection was the example of the disorder presented by Crocker and Pernet [36] (1907-1908) involving the same patient who had been the subject of Anthony's report on parakeratosis variegata two years before (1906). Pernet [26] believed the condition was related to *érythrodermie pityriasique en plaques disséminées*; Crocker regarded it as allied to xantho-erythroderma perstans, and Pringle ruled out early mycosis fungoides because there was no itching or infiltration. Pernet gave six roentgen treatments to a pink patch under the left nipple, and practically complete involution had resulted when the patient was presented. The condition and opinions on it remained the same, and Pernet's diagnosis had been

36. Crocker, H. R., and Pernet, G.: Case for Diagnosis, Proc. Roy. Soc. Med. (Dermat. Sect.) **1**:36, 1907-1908.

accepted by Arndt [1] when Pernet came to the United States two years later and discussed the report of Ravogli [37] (1910). At this time he [26] stated that he was inclined to regard Anthony's case as a probable instance of mycosis fungoides. In discussing the same paper, Hyde [13] stated that if he were called on to decide what was the most dangerous diagnosis for a dermatologist to make, he would say *érythrodermie en plaques disséminées.* He said he could recall several cases in which that diagnosis was made and which proved eventually to be instances of mycosis fungoides. The patient referred to by Dr. Duhring,[38] a distinguished former senator from a western state, in whose case the diagnosis of *érythyrodermie en plaques disséminées* had been made abroad, had been seen by Dr. Hyde within the preceding two or three months and exhibited unmistakable signs of mycosis fungoides. Thus, several transatlantic trips were necessary before a probable diagnosis of the condition in the cases of Pernet and Hyde became available in the literature.

In 1906 Civatte [3] published his comprehensive thesis on parapsoriasis. This article contains a mine of information on various phases of the subject and was written critically and with amazing frankness. Some of the outstanding points mentioned were: (1) that the primary lesion of parapsoriasis in patches is a macule; (2) that a pseudolichenified aspect was occasionally assumed; (3) that in many instances the dermatosis might disappear, though there might be subsequent relapses; (4) that tuberculosis was a probable etiologic factor; (5) that many conditions called parapsoriasis or a related disease were in reality examples of mycosis fungoides. Of the instances described by White,[24] Civatte expressed the belief that the first was acceptable as a case of parapsoriasis in patches, though reservations were made as to the possibility that it was one of early mycosis fungoides; that the second was, in reality, one of "premycosis," because of the infiltration of plaques on the legs, the slight pruritus, the intolerance of the skin, the iris-like figure on the right flank and the histologic picture, though the last was too banal to warrant a positive diagnosis; and, finally, that the third, involving a child, was one of seborrheid. In regard to the lesions described by Crocker,[23] Civatte went even further in announcing his belief in their premycotic nature, basing his contention on what he believed to be two revealing attributes: (1) the definite infiltration of many of the patches and (2) the description in some instances of peculiarly configurated lesions, the *marques de doigts,* which recalled to him the tendency of premycotic eruptions to form figures and geographic

37. Ravogli, A.: A Case of Erythroderma Squamosum (Parapsoriasis), J. Cutan. Dis. **28**:174, 1910.

38. Duhring, L., in discussion on Ravogli.[37]

shapes. These points caused him to deny the relation of xantho-erythroderma perstans to Brocq's parapsoriasis en plaques. In support of his view he quoted the dissenting opinions of several French dermatologists who had observed Crocker's first case and, in addition, cited protocols of three cases regarded clinically as involving conditions allied to xantho-erythroderma perstans but which he considered examples of mycosis fungoides. In the first of these cases Brocq had hesitated at first between the diagnosis of parapsoriasis en plaques and that of erythrodermic mycosis fungoides, but after three years of observation Civatte unconditionally rejected the former diagnosis. The second patient was shown to him by Darier, who demonstrated the case as a "probable case of what one calls parapsoriasis," stating that he was not convinced of the accuracy of such a diagnosis as applied to the condition of that patient. The histologic alterations were "extremely mild and almost insignificant"; yet on the basis of some infiltrated lesions and the general appearance of the dermatosis, Civatte classed the condition as premycotic. The last case was observed by Brocq, who regarded it tentatively as one of parapsoriasis. On clinical grounds, however, Civatte considered the condition early mycosis fungoides, though itching was not present. The interesting feature was the complete disappearance of the generalized eruption and the freedom of the body from lesions for some six months after the initial observation, a not uncommon feature of incipient mycosis fungoides. It will be seen, therefore, that in 1906 Civatte relegated Crocker's xantho-erythroderma perstans to the group of "premycotic" dermatoses.

The entity lichen variegatus (or parakeratosis variegata) experienced a similar fate when Civatte analyzed the data available to him. Indeed, he recorded an instance of parakeratosis variegata, which he regarded clinically as a case of mycosis fungoides and in which histologic examination revealed alterations consistent with the latter diagnosis.

In addition, Civatte reported three personally observed cases of parapsoriasis in patches. Without questioning the diagnosis of these cases I must state that the second and third patients (observations 9 and 10 in his thesis) were observed for only a short time. The condition of the first patient (observation 8 in the thesis) was most unusual clinically, exhibiting a peculiar eruption that recurred incessantly for several years; in four years of direct observation there were four attacks, each clearing completely in several months, and the last remission having a duration of at least one year at the time the thesis was written. In addition to this deviation from the description given by Brocq, there were interspersed attacks of urticaria on several occasions.

Some of the lesions were at one time described as urticarial and elevated, and once a patch of papulovesicular eczema appeared on the left forearm.

In 1929 Civatte,[20] discussing the subject of parapsoriasis, remarked:

> As for me, I have seen and followed a case classified as one of parapsoriasis "lichenoides" by Brocq and as one of poikiloderma of Jacobi by one of my German colleagues. Now, the patient had already had some tumors, and he died of mycosis fungoides. The reticulated atrophy was in him a premycotic lesion. . . .

Whether these remarks referred to the case of parakeratosis variegata described in his thesis in 1906 it is impossible to state; it may have been another case.

In the following year (1930) Milian and Lereboullet[10] recorded a case in which *érythrodermie pityriasique en plaques* terminated in the clinical picture of mycosis fungoides. Relative to this interesting example, Civatte made the succeeding important remarks:

> I wish only to support what Milian has just said, namely, cases of transformation of *érythrodermie pityriasique* into mycosis fungoides are infinitely rare, if they even exist. For more than twenty years, on the basis of readings perhaps badly interpreted, I have sought proof of this transformation; but I have followed for long years patients attacked by *érythrodermie en plaques* without seeing the condition in any case change into mycosis fungoides. The case that Milian has presented would, consequently, be of great interest if we were certain that there had been an initial stage in which none of the plaques had the least infiltration. . . .

But six years later (1936) Civatte[2] in a general article on parapsoriasis made several interesting statements indicating a tendency toward revision of his opinion on many fundamental aspects of the subject. The hypothesis that tuberculosis is an etiologic factor in parapsoriasis was now relegated to a minor position if not denied by implication. More important was the assimilation of Crocker's xantho-erythroderma perstans into the category of parapsoriasis en plaques, which, contrary to his views in 1906, now appeared justified. Especially interesting was his discussion of the reticulated form of Brocq's disease and the separation from it of lichenoid parapsoriasis, with parakeratosis variegata as a subvariety of the latter condition. He stated that the prognosis of parapsoriasis en plaques is "without real gravity, at least in practice," although he cited Milian's case in which transformation into mycosis fungoides took place and the warnings of Gougerot and Brocq of the possibility of such an occurrence. However, the entire question was left open when he stated:

> It will be seen further on that the histology supports with some arguments this menace of transformation into mycosis fungoides. It is then possible to make reservations in this connection. But one will recall that the fears which had been formerly expressed on this matter have been only very rarely justified.

In the section devoted to the minute anatomic picture, Civatte described two interesting features observed in some of his cases: (1) formation of what he called micro-alveolar spongiosis, or tiny spaces in the lower layers of the epidermis containing restricted numbers of lymphocytes or monocytes; (2) larger vesicle-like spaces in the inferior portion of the spinous layer, filled with cells similar to those found in the dermal infiltrate (large lymphocytes and monocytes)—in other words, "the same picture that Darier described in mycosis fungoides." Civatte then added:

> There are consequently, in parapsoriasis en plaques two microscopic alterations which appear to connect it with mycosis fungoides. This fact deserves to be remembered: I have already said that Milian observed the transformation of parapsoriasis en plaques into mycosis fungoides; on the other hand, one will find again these two histologic appearances in parapsoriasis lichenoides, and one knows that in certain cases parapsoriasis lichenoides is transformed into mycosis or, at least, into a condition very closely related.

Finally, in discussing the vexing problem of differential diagnosis from mycosis fungoides, Civatte confined his remarks to the following generalities:

> There is no difficulty in distinguishing parapsoriasis en plaques from the eczemato-lichenified, more or less infiltrated and frightfully pruritic eruption that ordinarily is the prelude to the appearance of tumors in mycosis. But it is not possible to affirm that the parapsoriasis en plaques which one has under one's eyes will not one day become transformed into a classic mycosis. In that respect one can no longer do more than make a calculation based on probability and reckon, as has been said above, that such an evolution is seen very rarely. We are ignorant of the nature of mycosis, and we know only that it is preceded by erythrodermas of variable type; it is possible—and certain histologic lesions of parapsoriasis en plaques furnish an argument in support of this hypothesis—that parapsoriasis en plaques, or at least certain types of parapsoriasis, are attenuated forms and classic mycosis the grave form of the same disease. But these are pure hypotheses which cannot be interposed in a diagnosis.

It can now be seen from the quotations given thus far that Civatte had not taken into full consideration the data found in the literature of other countries concerning the final outcome of parapsoriasis en plaques, parapsoriasis "lichenoides" and parakeratosis variegata.

In 1910 there appeared Arndt's article,[1] considered by many as the most authoritative exposition on the subject of parapsoriasis in patches. In order to separate this malady from others thrown into the general group of parapsoriasis, he advocated the title Brocq's disease. Besides a complete discussion of the literature Arndt included the detailed protocols of eight cases encountered by him during one and one-fourth years. Several outstanding points become evident when the recorded data are subjected to analysis: 1. The cases were observed only for a short time, in no instance beyond a period of one and one-half years. 2. There were accepted as authentic instances of Brocq's disease cases

in which the condition subsequently proved to be mycosis fungoides—for example, the case reported jointly by Crocker and Pernet.[36] 3. Many features exhibited in his cases were at variance with the criteria set down by Brocq—for example, in his second case complete disappearance of the eruption occurred under sulfur therapy and the skin was still normal some thirteen months after the original physical examination. 4. In many cases the descriptions were remarkably suggestive of incipient mycosis fungoides—for example, patches assuming the shapes of rings, semicircles and polycyclic figures were noted in case 3, central healing leading to formation of irregular rings in cases 4 and 8, figures-of-eight and horseshoe-shaped configurations in case 5 and sharply circumscribed foci bearing the shape of figures-of-eight, with parts of larger lesions revealing elevation above the surface in case 7. 5. In the only photograph demonstrating the histologic features the alterations (marked infiltration confined to the upper third of the cutis, with a well demarcated inferior limit, definite polymorphism of cellular components, dilated vessels in the papillary zone and proliferation of the rete pegs) appear, so far as one can surmise, to be consistent with the diagnosis of probable mycosis fungoides. However, mitotic figures were few. 6. In the elaborate exposition of the differential diagnosis from mycosis fungoides, exceptions can be found to all the points mentioned. 7. An eclectic description of parapsoriasis in patches was formulated on the basis of cases in which the accuracy of the diagnosis was not beyond cavil. As a result one finds in many modern accounts mention of central healing, for example, and perhaps of the formation of figures in this malady, though most authors state that such phenomena are but rarely encountered. Finally, it may be of interest to note that the eighth case in Arndt's article may well have been that of the patient to whom Hyde referred when he discussed the transition of érythrodermie en plaques into mycosis fungoides; this is, however, mere conjecture.

It would appear from this account of the early contributions to the subject of parapsoriasis that the conception of this disease has been based on evidence which calls for renewed evaluation. Few persons have taken the time and the trouble to apply the principle of follow-up in an effort to establish the authenticity of diagnoses in recorded cases. Even limited application of this principle has disclosed interesting results, indicating that the relation of this disorder to incipient mycosis fungoides is closer than usually has been assumed. The occurrence of authentic instances of parapsoriasis in patches being granted, however, the question then arises: Are there clinical or pathologic criteria permitting differentiation from early mycosis fungoides? The problem of differentiating cases of parapsoriasis in patches from those of seborrheic eczema, psoriasis, atypical pityriasis rubra pilaris, lichen scrofulosus and pseudo-xanthoma elasticum will not be considered.

DIFFERENTIATION BETWEEN PARAPSORIASIS IN PATCHES AND INCIPIENT MYCOSIS FUNGOIDES

Numerous authorities (Wise and Rosen, Brocq, Arndt and Civatte among others) have stated that parapsoriasis in patches and incipient mycosis fungoides can be differentiated in the early stages and have laid down criteria that appear well established. It is my belief, however, that this is not the case, as there are numerous exceptions to all the prescribed rules; even histologic examination, by many considered decisive, does not present an absolute criterion in all cases. These points have already been briefly indicated, and it now remains to delve into the matter in greater detail.

A. *Clinical.*—1. Infiltration: It is widely accepted that infiltration is encountered in the lesions of mycosis fungoides, whereas those of parapsoriasis in patches are distinguished by the absence of this attribute (Brocq [39]). There are, however, many examples of incipient mycosis fungoides, among them those reported by Juliusberg [4] and Gougerot and Burnier,[9] in which the characteristic infiltration does not appear on clinical examination. On the other hand, numerous alleged instances of parapsoriasis en plaques are recorded in which one or many lesions reveal definite clinical firmness (Crocker's case of xantho-erythroderma perstans, White's case 2, Wise's case 2 [40] and Bering's [41] case, among others). Indeed, Arndt noted that histologic examination may disclose cellular collections in the cutis out of all proportion to the minimal amount or the absence of clinical infiltration. Contrary to the opinion of Civatte, who believed there was no thickening of the skin apart from that caused by pathologic alterations in the epidermis, Arndt stated that moderate thickening of the skin, whether attributable to epithelial proliferation, infiltration of the cutis or both, is no basis for denial of the diagnosis of *érythrodermie pityriasique en plaques disséminées.* This is at variance with one of the cardinal tenets of Brocq's conception of the disorder.

As a corollary, the presence of cellular infiltration in the cutis is believed to explain the sharp contour and the circumscribed character of lesions observed in mycosis fungoides. There are, however, examples of this disease, in its incipient stage at least, in which poorly defined patches are exhibited (Juliusberg) and, contrariwise, alleged instances of parapsoriasis en plaques with lesions showing well demarcated borders (Arndt). Superficial "lichenification" and the formation of pseudopapules may be encountered in both disorders.

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39. Brocq.[6] Brocq.[33]

40. Wise, F.: Parapsoriasis, New York M. J. **102**:1032, 1915.

41. Bering, F.: Xantho-erythrodermia, in Neisser, A., and Jacobi, E.: Ikonographia dermatologia, Berlin, Urban & Schwarzenberg, 1910, p. 261.

Infiltration and its secondary phenomena are therefore insufficient means of differentiating these diseases in their incipient stages. Absence of marked thickening of the skin does not eliminate, by any means, the possibility of early mycosis fungoides.

2. Pruritus: Pruritus has been made one of the principal points in the differential diagnosis between these conditions. It is stated, for example, that in mycosis fungoides itching is persistent and usually intense to the point of intolerance (*pruritus frénétique*), whereas this feature is absent or markedly attenuated in parapsoriasis en plaques. However, instances of incipient mycosis fungoides unaccompanied by any itching or associated with mild, insignificant or minimal pruritus have been reported by Gougerot, Blum and Eliascheff,[42] Juliusberg,[4] Gougerot and Carteaud,[43] Riecke [44] and many others. Contrariwise, cases of parapsoriasis in patches have been described in which itching could hardly be considered an unimportant symptom (Kissmeyer [5]). Indeed, Wise and Rosen [11] declared: "It is fair to state, therefore, that the presence or absence of pruritus is not really a dependable symptom in the differentiation of the two dermatoses."

3. Polymorphism and Fixity of the Entire Eruption: One of the fundamental postulates to the recognition of parapsoriasis in patches is the chronicity of the dermatosis, with little or no tendency to disappearance or to morphologic change. According to Riecke,[44] this rule is entirely too rigid. In many of the recorded cases of parapsoriasis en plaques (Civatte's observation 8, Crocker's case 4, Arndt's case 2 and Kissmeyer's case, among others) the eruption disappeared for variable periods. In some cases the dermatosis may simulate psoriasis by undergoing involution during the summer and reappearing in the winter (Brocq, White). In still other instances the lesions may fade for variable periods, only to be succeeded by a more persistent eruption (Riecke). The relation of parapsoriasis in patches to therapy will be discussed under a separate heading.

On the other hand, mycosis fungoides is frequently attended by manifestations of variable appearance and comparatively short duration; it is the rule, apparently, for old lesions to undergo involution and to be succeeded by fresh patches of the same or a different type. Polymorphism of the eruption is therefore revealed either in the first attack

42. Gougerot, H.; Blum, P., and Eliascheff, O.: Deux cas de prémycose fungoïde sans pruritus, Arch. dermat.-syph. de la clin. Hôp. St. Louis **1**:604, 1929.

43. Gougerot, H., and Carteaud, A.: Prémycose à forme de parakératose (parakératose prémycosique); Puis de parapsoriasis, Arch. dermat.-syph. de la clin. Hôp. St. Louis **8**:114, 1936.

44. Riecke, E.: Ueber die sogenannte Parapsoriasis mit besonderer Berücksichtigung der Erythrodermia maculosa perstans, Arch. f. Dermat. u. Syph. **131**: 480, 1921.

of the disease or in subsequent relapses. To this excellent general rule, there are, however, exceptions—cases in which the fixed lesions remain over long periods—and to this variety of the condition scant attention has been paid. Juliusberg [4] and Nanta [45] among others have noted instances in which the dermatosis persisted unchanged for many years before transformation into the typical stage of raised plaques and tumors. Trimble [46] described a "premycotic" eruption which had been present unaltered for about twenty-five years. In the case recorded in this paper the lesions remained in the same form for about eight years.

Interesting, also, are those cases of alleged parapsoriasis in patches in which definite polymorphism was noted, owing to the formation of iris-like patches (White's [24] case 2, Wise's [40] case 2). Other features contributing to the appearance of polymorphism will be discussed under separate headings.

It will be seen, then, that the occurrence of a chronic eruption with persistently unaltered patches does not militate against the possibility of mycosis fungoides. Numerous instances of so-called parapsoriasis and its congeners have been reported (by Unna, Santi and Pollitzer, Gougerot and Burnier, Veiel, etc.) in which the constancy of the eruption and the fixed nature of the lesions composing it appeared to confirm the initial diagnosis of parapsoriasis or a related condition; yet these cases proved eventually to be examples of mycosis fungoides.

4. Color of Lesions: Kissmeyer [5] emphasized the yellowish color of lesions seen in parapsoriasis en plaques, contrasting it with the deep red observed in patches of mycosis fungoides. Other observers have noted the uniformity of color in the eruption of parapsoriasis in patches and the variations in hue exhibited by lesions of mycosis fungoides, but again, there are exceptions to these general rules. For example, Juliusberg [4] encountered instances of granuloma fungoides in which the patches were yellow, and—what is more significant—this attribute was persistent over periods of years. In my case the patient described the eruption at onset as resembling "liver spots" and remaining in this state for a long time before transformation into typical mycosis fungoides. There are instances of parapsoriasis in patches in which the individual lesions exhibited variations ranging from yellow to reddish blue. It will be seen, therefore, that no reliance can be placed on this criterion in differential diagnosis, particularly in the early stages of the condition.

45. Nanta, A.: Mycosis fungoïde, in Darier, J.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 5, p. 539.

46. Trimble, W. B.: The Chronic Scaly Erythrodermias, J. A. M. A. **53**: 264 (July 24) 1909; Private Notes on Several of the Rare Dermatoses, J. Cutan. Dis. **28**:186, 1910.

5. Central Healing of Lesions: According to Arndt,[1] islands of normal skin may be encountered within patches in occasional instances of *parapsoriasis en plaques disséminées,* causing the lesions to assume a circinate appearance; in his differential diagnosis from mycosis fungoides, he evaluated this attribute on the basis of intensity. In nearly all cases of parapsoriasis in patches which he observed there were exhibited, in addition, peculiarly shaped configurations, a clinical attribute tending to suggest the possibility of mycosis fungoides; indeed, the photographs of sections in one of these cases seem to support such a suggestion. Sherwell [12] reported an instance of *érythrodermie pityriasique en plaques disséminées* (this may be the case cited by Ormsby [22] as an example of mycosis fungoides), in which some of the lesions had circinate outlines, with central spots "as of sound or cured skin"; nearly all the men who observed the case at the demonstration expressed their belief in the "premycotic" nature of the eruption, while those who dissented used reasons now regarded as fallacious. Civatte noted that the occurrence of circinate configurations is a rare phenomenon, and Juliusberg mentioned the occasional formation of medallions, but it seems probable that these notations are based, for the most part, on descriptions recorded in the literature by other observers.

It will be seen, therefore, that the occurrence of central healing and the formation of peculiar figures characteristic of mycosis fungoides have been recorded in alleged examples of parapsoriasis in patches. Whether the differential diagnosis can be made on the basis of differences in degree, as stated by Arndt, seems doubtful in the light of the data collected.

6. Location of Lesions: The eruption in parapsoriasis en plaques shows a definite predilection for the trunk and the limbs. In the earlier descriptions it was stated that the face, the scalp, the backs of the hands and the feet were rarely affected and the palms and soles never (Arndt). Subsequent observations have disclosed instances in which lesions were encountered on the face (for example, Heller's [47] case 4, Crocker's case 1, J. C. White's case 1, the cases of Callomon,[48] of Gougerot, Meyer Eliascheff, of Unna, Santi and Pollitzer, and of Rosen, my case and others); on the scalp (reported by Bering [41] and Riecke [44]), and on the backs of the hands (reported by Ravogli [37]). Of these examples it has been found that mycosis fungoides developed in instances reported by

47. Heller, F.: Ueber die Beziehungen der Parapsoriasis en gouttes zu der Brocqschen Krankheit, Arch. f. Dermat. u. Syph. **108**:71, 1911.

48. Callomon: Zur Kenntnis der Brocqschen Krankheit, Arch. f. Dermat. u. Syph. **114**:503, 1912. This case was classified as one of mycosis fungoides by Herxheimer, K., and Martin, H., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 8, pt. 1, p. 178.

Gougerot, Meyer and Eliascheff, by Unna, Santi and Pollitzer, by Rosen, by Keil and probably by Callomon.[48] In addition, there have been instances in which the original eruption was restricted to the trunk or to the limbs and subsequently appeared on the face, when the diagnosis of mycosis fungoides was established (Gougerot and Burnier).

It will be seen, then, that the localization of an eruption on the trunk or on the limbs, even for many years, does not militate against the diagnosis of incipient mycosis fungoides. It would seem that the appearance of facial lesions occurs not uncommonly in cases in which the clinical picture of mycosis fungoides eventually develops.

7. Duration of Entire Eruption: There have been recorded a few instances in which parapsoriasis in patches had a duration measured in decades (Crocker's [23] case 5, thirty years, and the cases of Wise [21a] from twenty to twenty-five years, of Ormsby,[22] sixteen years, of Bogrow,[49] forty years, and of Rasch,[50] about fifty years). With the exception of the patients mentioned by Wise and Ormsby, no case was observed for a long period, the total duration of the dermatosis having been computed on the basis of information given by the patient. It is interesting that in Bogrow's [49] case there was an unexplained proportion of eosinophils of 13.1 per cent. It is likewise of great interest that the patient mentioned by Wise [21a] (1934) was the one presented by Pollitzer [21b] in 1911. On the latter occasion Drs. G. H. Fox, Corlett, Trimble and Veiel diagnosed the condition as incipient mycosis fungoides, and Pusey and Engman, in agreement with Pollitzer, as parapsoriasis in patches. Ravogli and White were noncommittal. This patient presented one large lesion covering almost half the circumference of the left thigh, several circular and irregular patches and a few distinctly but superficially infiltrated plaques.

On the other hand, occasionally incipient mycosis fungoides may go on for a long period without much change in the lesions, significant pruritus or impairment of the general health. Examples of this type have been recorded by Trimble, Nanta and Juliusberg. There are cases, too, such as the one described so admirably by Gougerot and Burnier, in which the initial diagnosis was parapsoriasis in patches; yet some twenty-two years after onset the clinical picture was undoubtedly that of mycosis fungoides.

8. Impairment of General Health: From the foregoing remarks it will be seen that the maintenance of general good health, even over long periods, does not eliminate the possibility of incipient mycosis fungoides.

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49. Bogrow, S. L.: Zur Klinik und Diagnose der Parapsoriasis en plaques (Brocq), Dermat. Ztschr. **18**:137, 1911.

50. Rasch, C.: Pityriasis maculosa chronica (érythrodermie pityriastique en plaques disséminées), Dermat. Ztschr. **10**:594, 1903.

9. Glandular Involvement: The example of xantho-erythroderma perstans of "premycotic origin" recorded by Milian and Perin [51] is of interest because lymphadenopathy was one of the principal points in favor of that diagnosis. The eruption had been present for three and one-half years on the limbs, sparing the trunk and the face; the color of the lesions was that of xantho-erythroderma, and there was marked inguinal adenopathy, accompanied with small mastoid, submaxillary, postcervical and axillary glands. Some of the plaques were infiltrated. The histologic picture was considered consistent with the diagnosis of mycosis fungoides in the early stage. There were 12,500 white blood cells, with 9 per cent eosinophils. It is interesting to note that in the case described by White [52] there was a relatively slight symmetrical involvement of the epitrochlear and axillary lymph nodes, the significance of which was not clear.

10. Response to Therapy: Among the principal characteristics displayed by eruptions of parapsoriasis in patches is the failure to respond to therapeutic measures of various types. To this rule numerous exceptions have been recorded. Lesions have apparently undergone complete involution after local medication in cases reported by Arndt, Wise, Civatte and many others; partial disappearance has been seen in instances described by Bogrow, Kissmeyer and Crocker, among others. In the case reported by Bering, there appeared to be a definite tendency to spontaneous recovery, since untreated as well as treated patches underwent involution. Chipman [53] and others have noted instances in which ultraviolet rays caused disappearance, followed by relapse when irradiation was discontinued. The tendency to spontaneous recovery has been stressed by Riecke, who, moreover, denied the value of sulfur, of ultraviolet rays and of pilocarpine. In the case recorded in this paper some four years after onset the eruption refused to yield to a variety of therapeutic measures, including local applications, ultraviolet rays and a few exposures of roentgen rays; yet, subsequently, when the clinical picture of mycosis fungoides was well established, there was prompt response to small doses of roentgen rays. It has been noted by Juliusberg that in some cases incipient mycosis fungoides seems to respond with difficulty, if at all, to roentgen therapy, at least in the beginning. My case probably is one of those.

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51. Milian, G., and Perin: Xantho-érythrodermie (Érythrodermie prémycosique probable) en plaques avec hyperkératose, Bull. Soc. franç. de dermat. et syph. **31**:466, 1924.

52. White, C. J.: Érythrodermie Pityriasique en Plaques Disséminées, J. Cutan. Dis. **21**:153, 1903.

53. Chipman, E. D.: Parapsoriasis, Arch. Dermat. & Syph. **4**:807 (Dec.) 1921.

It seems, then, that failure to yield to various therapeutic agents, including roentgen rays, does not entirely eliminate the possibility of mycosis fungoides, especially in the early stages. The capriciousness and the tendency to spontaneous involution shown in some cases of parapsoriasis en plaques call to mind some of the principal attributes of mycosis fungoides. It would be of interest to know the specific effect of intensive roentgen treatment of patches of parapsoriasis en plaques.

11. Prognosis: It has already been indicated that the prognosis of parapsoriasis in patches is not as innocuous as one is led to believe from opinions recorded in the literature. If it is true that in some cases lesions may continue over many decades without impairing the general health and without causing pronounced pruritus, the same is equally true in occasional cases of mycosis fungoides. It would appear that parapsoriasis in patches can hardly be considered a mere cosmetic blemish. There is evidence which, if not absolutely conclusive, at least strongly suggests that parapsoriasis en plaques and incipient mycosis fungoides stand in closer relation to one another than has been hitherto believed.

B. *Histologic Examination.*—Histologic diagnosis presents innumerable difficulties owing to (1) the inclusion in the records of cases in which parapsoriasis in patches eventually was transformed into mycosis fungoides, unbeknown to the pathologist, who relied on the original clinical diagnosis, and (2) the attempt to see analogies to other conditions having in common the name parapsoriasis, such as the en goutte variety (pityriasis lichenoides chronica).

1. Epidermal Changes: Some authors, while not regarding epidermal alterations as primary, nevertheless consider them relatively distinctive. Opinions are, however, not unanimous on this point. According to Gans, whose account is based principally on that of Arndt, the granular layer may be missing in areas showing edema of the epidermis and some wandering cells, with replacement by parakeratotic scales; on the other hand, Civatte stated that the granular layer is unaffected. Some authors speak of moderate epithelial proliferation, accompanied with some lengthening of the rete pegs; others note that such changes are minimal or absent, and still others speak of atrophy of the epidermis late in the course, attributing this alteration to the pressure of edematous fluid. Moderate intercellular and intracellular edema have been described. Especially important are the two appearances recorded by Civatte as suggesting an alliance with mycosis fungoides: (*a*) micro-alveolar spongiosis; (*b*) vesicle-like spaces containing lymphocytes and larger monocytes, the latter being analogous to the condition described by Darier in incipient mycosis fungoides. These alterations have already been mentioned briefly.

2. Changes in the Cutis: There are mild infiltration of lymphocytes and proliferating connective tissue cells about the subpapillary vessels and some diffusion of these cells in the papillary bodies. This has been described in many reports, but the changes are considered banal. On the other hand, Arndt showed photomicrographs in a case of parapsorias in patches in which the cellular collections were fairly polymorphous and the rete pegs prolonged to a greater extent than is usual. Mitoses were scarce. In Arndt's case there was a well defined infiltration occupying the entire upper third of the cutis, the inferior limit of which was sharply demarcated—another unusual appearance when it is considered that most authors have described the infiltration as ill defined.

It is my belief that these alterations may be encountered in the early stages of mycosis fungoides before the characteristic changes have appeared. It is now widely accepted that the incipient stages of this condition may be marked by the appearance of banal alterations (Gans,[54] Darier and others); for example, in the case reported in this paper, three separate histologic examinations made in 1932 and 1933 failed to show a picture consistent with a diagnosis of early mycosis fungoides (this has recently been corroborated by a number of independent observers); yet, in 1936 the specific alterations of mycosis fungoides were encountered. To illustrate the point more forcefully, the original findings in the case reported by Rosen were those of "retrogressing or quiescent parapsoriasis"; yet, more recent examinations indicated the likelihood of mycosis fungoides. Finally, it had been noted by Arndt that the cellular infiltration in the cutis might be out of all proportion to the degree of clinical infiltration; that point seemed to be well shown by the two photomicrographs published with his article, which revealed an appearance most unusual for ordinary parapsoriasis in patches and rather more consistent with the picture of incipient mycosis fungoides. Similarly, there have been instances of mycosis fungoides in which are exhibited patches that are not infiltrated or are only superficially thickened (therefore indistinguishable from parapsoriasis en plaques) but in which the minute anatomic picture was definitely that of mycosis fungoides. Such a case was reported by Wise and Rosen. In such instances the histologic examination clarifies obscurities in the clinical picture, but when the alterations are banal, like those previously described, extended observations have shown that the diagnosis of mycosis fungoides cannot be eliminated with absolute certainty, and the classification of the case will depend, in great measure, on follow-up.

54. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 312.

SUMMARY

The classification of parapsoriasis, on which few agree, is said to embrace the following conditions:

1. Parapsoriasis en gouttes or pityriasis lichenoides chronica (Juliusberg). The precise relation of this condition to "parapsoriasis varioliformis" (Mucha-Habermann) is as yet not clear.

2. Parapsoriasis "lichenoides" (Brocq), which is considered to be the equivalent of parakeratosis variegata (Unna, Santi and Pollitzer).

3. Parapsoriasis in patches (*érythrodermie pityriasique en plaques disséminées*).

4. Retiform parapsoriasis, which has been variously classified in group 2 or group 3 or as an independent entity. Cases of this type, as well as those of parakeratosis variegata (parapsoriasis "lichenoides" of Brocq) have been diagnosed more frequently during the past few years as examples of poikiloderma.

Although in occasional instances transitions between these various types have been described by several observers, many authorities (Civatte, Juliusberg and Jadassohn, for instance) have not been convinced of their authenticity; others, such as Kissmeyer, have expressed the belief that these eruptions and their morphologic attributes can be interpreted differently. In any event, such examples are rare.

Of the types enumerated, the second, third and probably the fourth are often complicated by the appearance of mycosis fungoides; in at least this sense they seem to be related. The clinical evidence of transition between these three varieties is far more conclusive than that in parapsoriasis en gouttes, which does not appear ever to be succeeded by mycosis fungoides, so far as can be ascertained from perusal of the literature and personal observation of cases. It would seem that the condition called pityriasis lichenoides chronica and its possible ally parapsoriasis varioliformis are distinct entities that ought to be separated more definitely from the other variants of "parapsoriasis."

CONCLUSIONS

There is evidence that parapsoriasis en plaques becomes complicated by mycosis fungoides after variable periods, in some cases after decades. This happens in so large a percentage of instances as to invite the belief that parapsoriasis in patches and its clinical congeners are probably, in most if not in all cases, the precursors of mycosis fungoides. This form cannot be regarded as "attenuated" mycosis fungoides (Civatte), since the tendency to last for many years holds equally for other clinical

varieties of mycosis fungoides. In support of these views, the following evidence may be cited:

1. Study of the original papers on which the conception of parapsoriasis in patches was founded seems to indicate that cases which could be followed or observed adequately turned out to be examples of incipient mycosis fungoides. The evidence appears to speak clearly against the hypothesis that the two conditions are merely coincidental.

2. Study of differential diagnostic criteria hitherto considered decisive discloses that these disorders cannot be distinguished on clinicopathologic grounds early in their course.

3. Study of one case and of reports of a large number of others of parapsoriasis in patches and its allies in which the condition ultimately developed into mycosis fungoides reveals the important point that the original eruption conformed in nearly all instances to the postulates laid down by Brocq. In many such cases the initial pathologic alterations were those commonly regarded as nonspecific or as supporting the diagnosis of parapsoriasis in patches.

4. The syndrome of parapsoriasis en plaques followed after a variable period by alterations of the nature of poikiloderma suggests early mycosis fungoides.

5. In agreement with views propounded by a number of authorities, such as Gans, Darier and others, it appears that in many examples of incipient mycosis fungoides the minute anatomic changes are so banal as to render recognition of this disease difficult, if not impossible, early in the course. As pointed out by Juliusberg, there are cases in which incipient mycosis fungoides shows clinical features of parapsoriasis in patches, nonspecific histologic changes and even refractoriness to roentgen therapy, at least in the beginning.

6. Parapsoriasis in patches is not merely an innocuous cosmetic blemish of the skin, even when it has remained unaltered for many years. The data reviewed in the text disclose how frequently this condition becomes transformed into mycosis fungoides.

7. The histologic criteria for the recognition of parapsoriasis in patches and of incipient mycosis fungoides deserve fresh study in the light of the data presented in this paper.

Clinical Notes

RECURRENT REACTION TO PATCH TEST

CLEMENT E. COUNTER, M.D., LONG BEACH, CALIF.

The purpose of this paper is to describe a phenomenon[1] in which the site of a positive reaction to a patch test becomes reddened again after having returned to normal. The second appearance of redness occurs without local contact but simultaneously with a new contact causing dermatitis elsewhere. No doubt this phenomenon has been observed before, but I have not seen it described.

REPORT OF CASES

CASE 1.—Mrs. F. had been complaining of sore hands for four months when I first saw her. The history of her cutaneous disorder showed that during the previous year she had been unable to wear a white gold wrist watch and white gold earrings because of local irritation produced by them.

Clinical examination revealed definite areas of erythematosquamous eruption, together with patches of vesiculation and crusting, on the backs of the hands and around the wrists.

Patch tests carried out immediately with a 5 per cent solution of nickel sulfate and with a 5 cent piece produced reactions with vesiculation. These reactions remained visible for ten days but had disappeared at the end of fifteen days.

After six weeks' treatment the patient's hands appeared normal, and she was warned concerning contacts with nickel objects and told that she need return only if she had a new attack. Two weeks later she returned, with a bright red papular eruption on the inner surfaces of both elbows, evidently produced by her nickel-trimmed pocketbook. Simultaneous with the eruption on her arms the areas of the two patch tests on her thigh became red and papular. This occurred after there had been no sign of a reaction for over four weeks and without any new local contact.

A week later the sites of the positive patch tests were only slightly visible, having improved along with the lesions on the arms.

CASE 2.—The second patient was a physician who had an eruption on his fingers. Medicines and solutions handled by him were suspected, and patch tests of these were made. The site of the test with procaine hydrochloride became red and swollen, but other tests gave negative results. The patient knew that he was sensitive to butyn, because it had produced severe conjunctivitis one year before, when it had been used in an eyewash. A patch test with butyn was not made at this time.

The positive reaction was observed on February 21. By March 10 the signs of a positive reaction were gone. On March 25 the patient was exposed to a 1 per cent solution of butyn in the course of administering a local anesthetic. The next day the fingers of his right hand became red and swollen, and he became conscious of tenderness on the left arm. Investigation showed that the site of the

1. Dr. Samuel Ayres Jr., of Los Angeles, called my attention to this phenomenon and suggested that a short report would be of interest.

positive reaction to procaine hydrochloride had become red and irritated again after having been normal for two weeks. The new reddening of the site showed about 80 per cent of the severity of the first reaction.

By avoiding both procaine hydrochloride and butyn improvement in the fingers was effected, and in two weeks they were normal in appearance. This second reaction test at the site of the patch with procaine hydrochloride disappeared in ten days.

COMMENT

These two cases are somewhat similar to a case studied by Gougerot and Brouet,[2] that of a patient who was sensitive to adhesive tape. Not only did a local reaction develop to the tape where it was applied, but redness and eczematization appeared on distant parts of the body. This occurred repeatedly, as the patient was studied experimentally. Gougerot and Brouet expressed the theory that the dermatitis, developing on a distant part of the body from the point at which the causative irritant had been applied, is to be explained by one of two hypotheses: Either some unknown autotoxic or exotoxic harmful substance fixes itself on cutaneous areas and sensitizes them, or the harmful material to be found in the specific substance is absorbed from the areas involved in the dermatitis and carried by the blood stream to other areas of the skin.

The reappearance of the local reaction at the site of a previous positive reaction to a patch test, along with the development of dermatitis on another part of the body, emphasizes the fact that there is an internal predisposition and that this internal influence affects widely separated cutaneous areas. It may be expected that if a patient has been exposed to an external substance to which he is sensitive and dermatitis has developed, he may have a new attack by a new contact, which will involve not only the skin newly irritated but other areas that were affected in the previous attack.

SUMMARY

Two cases are reported in which the site of a positive reaction to a patch test became definitely red and swollen again when a new contact had caused fresh dermatitis on a distant part of the body.

In one case the dermatitis, occurring simultaneously with the recurring redness at the site of the former positive reaction, was caused by the same substance which was used to produce the original positive reaction.

In the other case redness recurred at the site of a previously positive reaction at the same time that dermatitis occurred at a distant point. The dermatitis in the later attack was caused by contact with a different substance from that which produced the original positive reaction.

117 East Eighth Street.

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2. Gougerot and Brouet: Eczéma par sensibilization à l'emplâtré simple, d'abord localisé puis disséminé: Discussions pathogéniques, Bull. Soc. franç. de dermat. et syph. **42**:1599-1604 (Nov.) 1935.

News and Comment

POSTGRADUATE COURSE IN THE CONTROL OF SYPHILIS AND GONORRHEA

The Harvard School of Public Health is offering a postgraduate course in the control of syphilis and gonorrhea, in cooperation with the United States Public Health Service and the Massachusetts Department of Public Health, Division of Genitoinfectious Diseases.

The course will be of one academic year's duration. The next session will begin on Sept. 26, 1938. The course aims to give a broad training in syphilis and gonorrhea, including symptoms, diagnosis, treatment, control, prevention and public health aspects. Clinics have been arranged at the Massachusetts General Hospital, the Boston Dispensary, the Boston City Hospital, the Children's Hospital and the Boston Psychopathic Hospital. Laboratory work will be reviewed at the State Serological and Diagnostic Laboratories. Enough time will be spent with the state Department of Public Health to allow the student to become familiar with all public health aspects. Lectures on all phases of the subject will be given by clinicians, laboratory directors and public health officials.

Registration is open to physicians who are graduates of approved medical schools and who have had at least one year's internship in an approved hospital. The prospective student should first obtain the approval of his State Commissioner of Health and transmit this to the Commissioner of Public Health, State House, Boston.

Further information and blanks of application for admission may be obtained from the dean of Harvard School of Public Health, 55 Shattuck Street, Boston.

COURSE IN OCCUPATIONAL DERMATOSES

A course in occupational dermatoses will be given under the auspices of the Harvard School of Public Health during May 1938. Lectures will be given on clinical manifestations, etiology, diagnosis, treatment, insurance and legal aspects. Clinics will be held at the Massachusetts General Hospital and in association with various insurance companies. Visits to some of the more important factories will be arranged, so that students may study industrial processes and preventive measures. The number of students will be limited to ten. Further information and registration blanks may be obtained from the dean of Harvard School of Public Health, 55 Shattuck Street, Boston.

DEATHS

Dr. R. J. A. Sabouraud, of Paris, France, died on Feb. 5, 1938.

Prof. Otto Kren, of Vienna, Austria, died on Dec. 3, 1937.

PHYSICIANS' ART EXHIBIT

The American Physicians' Art Association, a national organization of physicians who have ability in the fine arts, will hold its first national exhibition in

the San Francisco Museum of Art, San Francisco, in June 1938. All entries must be in before April 1, 1938. Any physician interested should communicate at once with the secretary of the American Physicians' Art Association, Suite 521, 536 Flood Building, San Francisco.

CORRECTION

In the abstract of the report entitled "A Case for Diagnosis (Plummer-Vinson Syndrome [Microcytic Anemia]?), by Dr. Fred Wise, in the proceedings of the Nov. 10, 1936 meeting of the Manhattan Dermatologic Society, in the July issue (ARCH. DERMAT. & SYPH. **36**:155, 1937), reference was made to the presentation of the patient at the October 6 meeting of the New York Academy of Medicine, Section of Dermatology and Syphilis. The report was said to be on page 46 of the July issue; it appeared, however, on page 200.

Obituaries

SIGMUND POLLITZER, M.D.
1859–1937

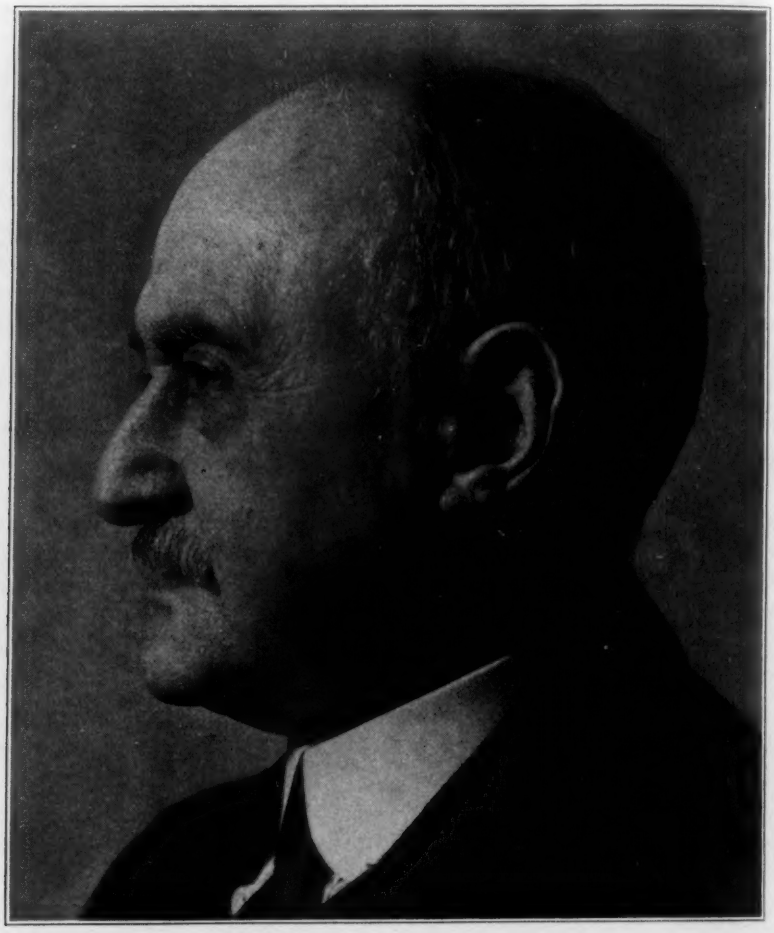
Sigmund Pollitzer, dermatologist of international preeminence, died on Nov. 1, 1937, after a brief illness, at the age of 78. Pollitzer was born on Staten Island, N. Y., on June 12, 1859. His parents came north from the little town of Beaufort, S. C., and it was here, under the private tutelage of a Harvard graduate, that Pollitzer received his early education. At the age of 13 he had read the works of Cicero and Virgil and was therefore well prepared to enter the College of the City of New York for his high school and college training. His early boyhood among the little islands of Port Royal Harbor was spent happily, as he himself said, with "boats, dogs, guns and horses." Although he spent the rest of his life in the North, his Southern background reflected itself in his later life in a generous hospitality and in a chivalrous spirit in his dealings with his fellows.

His early college days in New York brought him into close contact with Prof. Alfred G. Compton, of the City College, who directed his activities into the fields of physics, mathematics and astronomy, to which he devoted himself for almost three years. He graduated from the College of the City of New York in 1879, with honors and a Phi Beta Kappa key. In 1882 he received a master's degree from the same college. Pollitzer had a decided flair for mathematics, and at about this time he published a manual of logarithmic computation, which for many years enjoyed wide use, not only in financial affairs but as an aid in computing data for navigation.

Pollitzer's medical work was done at the Columbia University College of Physicians and Surgeons, from which institution he graduated in 1884. His thesis at graduation was an original piece of research, "Temperature Sense," which was published in the *British Journal of Physiology*. After graduation he went abroad and continued his research in physiology in Heidelberg, Germany. During his studies there he published two papers on physiologic subjects, one in *Pflueger's Archiv* in 1885 and the other in the *British Journal of Physiology* in 1886.

In 1885 he studied bacteriology and was among the first American students to be initiated into modern methods of bacteriologic research. These he learned in Fresenius' laboratory in Weisbaden, Germany, under Hueppe.

The summer of 1885 found him in Berlin, Germany, where he worked in Virchow's laboratory and occupied himself in general medical work. At this time he published the first piece of work on the nutritive value of peptone, the research for which had been done in Zuntz' laboratory. From Berlin he traveled to Vienna, Austria, where he continued



SIGMUND POLLITZER, M.D.
1859–1937

the study of clinical medicine. At this time, when war broke out between Serbia and Bulgaria in the fall of 1885, he volunteered for service with the Serbians and became head of a reserve hospital at Passowitz, and later of one at Zaitchar. At the close of hostilities he was discharged with the rank of major.

In the spring of the following year he returned to New York and entered the practice of medicine. In spite of his excellent preparation, patients were few, and after three years of struggle Pollitzer gave up the field of general medicine for the field in which he achieved international distinction. In 1889 he again went abroad and became a member of a famous group of foreign students in the Unna clinic, where he remained for one year. With him at that time were four fellow students who achieved international reputations—Török, Philippson, Mibelli and Tomasoli. With these Pollitzer maintained an active friendship over many years.

Of the many pupils of the Unna school, Pollitzer was always regarded by the old master as the outstanding one. It cannot, however, be truthfully said that Pollitzer remained an adherent of any one school. A student of English, French, Austrian and German dermatologic theories, he absorbed the soundest ideas of each school and evolved a scientific and clinical credo of his own. From Unna's clinic he went to London, England, where he became an assistant of Malcolm Morris and for a time edited the *British Journal of Dermatology* under Morris' direction. He attended the various clinics of London and laid the foundations for a lasting friendship not only with Morris but with Pringle and Colcott Fox.

From London he went to Paris, France, where began a close association and friendship with Darier, which lasted up to the time of his death. Of all his foreign contacts, that with Darier was the closest, and these two contemporaries carried on an active correspondence in dermatologic affairs throughout the almost fifty years of their friendship. In 1920 Pollitzer translated and edited Darier's "Précis de dermatologie," the original of which Pollitzer always regarded as a valuable and unique treatise on dermatology.

In the summer of 1890 Pollitzer acted as one of the secretaries of the dermatologic section of the Tenth International Medical Congress at Berlin, Germany, and in the fall of that year he returned to New York, where he established himself as a practitioner of dermatology, for which he was admirably fitted by his long apprenticeship not only in his special field but in the fields of general medicine, physics and chemistry.

In New York he practiced dermatology for forty-seven years. In 1895 he became professor of dermatology at the New York Post-Graduate Medical School and Hospital, a position which he held until 1915. He was also chief of clinic at the German Hospital Dispensary and consulting dermatologist to the Beth Israel and the Lenox Hill hospital.

In New York he was actively associated with the New York Academy of Medicine, the dermatologic section of which he took an

active part in establishing, and he was in no small way responsible for the splendid forum which this section maintained for many years. He took an active part in the discussions and contributed in a large way to the education of the young dermatologists who took advantage of the rich material and the entertaining and interesting meetings of the section. He evinced an even greater interest in and was ever a loyal supporter of the American Dermatological Association, to which he was elected in 1896 and of which he became vice president in 1913 and president in 1914. The incorporation of the American Dermatological Association in 1930 was due in large part to his tireless efforts.

During the World War, Pollitzer served as major in the medical corps, first as consultant in the surgeon general's office in Washington and later at base hospital no. 1 in the Bronx.

He was an active alumnus of the New York City College and served both as vice president and as president of the alumni association, as a member of the finance committee, as president and trustee of the student aid association and as president of the college chapter of Phi Beta Kappa.

Pollitzer's contributions to dermatologic literature (seventy-one) were marked more by their outstanding character than by their number. All of them were written in faultless English and easy style and reflected admirably the keen analytic mind which characterized his diagnoses and his perpetual search for scientific truth. Especially noteworthy were his classic works on acanthosis nigricans, hydradenitis destruens suppurativa, parakeratosis variegata, naevus angiectodes disseminatus, the xanthomas, and the nature of xanthoma of the eyelid.

Pollitzer not only took an active interest in dermatology but was a syphilologist of excellent judgment. He was among the first to receive arsphenamine from Ehrlich, and his paper entitled "Salvarsan in Syphilis" was the first address on this subject before an American audience, being published in 1911. He was among the first to publish a paper on the serodiagnosis of syphilis. This appeared in 1907, under the title, "Serum Therapy and Serum Diagnosis in Syphilis."

In dermatologic societies Pollitzer will be remembered as a lively participant in discussion and a keen critic. He was intolerant of superficial work and of pure speculation. He never hesitated to speak his mind freely when work was presented which appeared to him to have little scientific foundation. His criticisms were never personal, if pertinent and sharp, and after a meeting at which he had been outspoken he always lapsed into a kindly, genial mood which took much of the sting out of his remarks. If his particular friends trod on thin ice, he belabored them especially, and those who have been so handled have realized through the years that Pollitzer's criticisms not only were attended with good intentions but were good lessons in medical straight thinking.

He was a strict adherent of parliamentary rules. This insistence on regular procedure not infrequently involved him in polemics from which he emerged more frequently in defeat than in victory. However, the honesty of his intention was never questioned, and it can truthfully be said of him that he always went down fighting for what he believed to be right.

It was in the atmosphere of his home, however, that Pollitzer was seen at his best. Those who enjoyed the intimacy of his delightful home life with his charming wife and two daughters appreciated the real kindliness and the generous spirit which so admirably complemented his energetic mind.

To dermatologists of the future Pollitzer's name will live as that of one of the pioneers who helped place his specialty on a dignified and sound basis. He enriched its literature and helped to put a confused group of morphologic pictures into their proper places in the field of medicine.

By his contemporaries he will be remembered as a man of fundamental intellectual integrity, a vigorous and earnest student and teacher, a forceful debater and an outstanding figure of his generation.

For the intimate group of those who knew and loved him as "Polly," the delightful simplicity of his life, his generous, loyal friendship and the nobility of his character remain treasured memories.

U. J. W.

CHARLES MORTON SMITH, M.D.

1867–1938

Morton Smith is dead, and his former colleagues and his patients, who always became his devoted friends, wonder who can fill his place.

Charles Morton Smith was born on Oct. 20, 1867, in Dublin, N. H., in the foothills of the White Mountains, the son of Charles J. Smith, mill owner and farmer, and Sarefta Culver Smith. In 1896, in Newburyport, Mass., he was married to Mary L. Moulton. A son and a daughter were born of this marriage. These three survive.

Morton Smith was graduated from the Academy in Pembroke, N. H., in 1889. That autumn he entered the Harvard Medical School, but before receiving his degree in medicine, in 1894, he served as surgical house officer at the Boston City Hospital in 1893 and 1894. This service, ordinarily of eighteen months' duration, was prolonged in his case to two years because of an intervening severe illness.

In 1894 he was appointed assistant physician to the department of dermatology at the Boston Dispensary, under Dr. Abner Post, and he remained at that institution until 1914. Meanwhile he worked as an assistant in the department of dermatology at the Boston City Hospital, serving from 1900 to 1905. In 1914 he was called to head the newly created department of syphilis at the Massachusetts General Hospital, with Dr. Abner Post as consultant. Here he remained until his retirement from all official hospital duties in 1926. To this clinic he gave all that was in him.

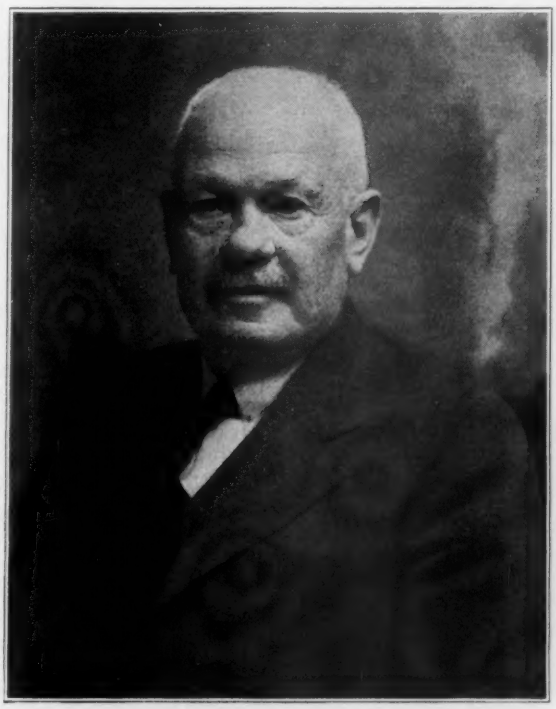
In the Harvard Medical School Morton Smith served as assistant professor of syphilis from 1916 to 1921, as clinical professor of syphilis from 1921 to 1926 and as clinical professor emeritus from 1926 until his death. In the Harvard Dental School he was instructor in syphilis from 1906 to 1917.

During the World War, in conjunction with the Surgeon General's office, he engaged in the teaching of medical officers recently appointed to the United States army, giving small groups intensive instruction in clinical dermatology.

Morton Smith joined the Massachusetts Medical Society in 1893, the American Medical Association in 1897 (?), the American Dermatological Association in 1913 and the New England Dermatological Society at its inception, in 1925. In the Massachusetts Medical Society he served as president of the Suffolk district from 1924 to 1926 and as chairman of the dermatologic section in 1936; in the American Dermatological

Association he became president in 1930; in the New England Dermatological Society he was president in 1926 and was president of the Atlantic Dermatological Conference in that same year.

As a writer Morton Smith was not prolific, but what he gave to the public in his written contributions was sensible, interesting, well digested and exact. In 1912 he published "The Relation of the Physician and the Social Worker in the Effort to Save Damaged Goods." The expression "damaged goods" was much in people's mouths, owing to



CHARLES MORTON SMITH, M.D.
1867-1938

a French play concerning syphilis written by Eugène Brieux in 1911, when even the word syphilis was taboo in polite society. In 1927 he published "One Thousand Cases of Congenital Syphilis." When this paper was read before the American Dermatological Association during the previous year, it was acclaimed as few papers have been within my recollection. "Twenty Years of Syphilis under Salvarsan" furnished another instance wherein this man's great experience was presented in a telling and valuable manner. A paper on interstitial keratitis, which was prepared in collaboration with Dr. George Derby, of the Massa-

chusetts Charitable Eye and Ear Infirmary, demonstrated once again this syphilographer's great powers of succinct analysis.

Morton Smith began his public medical career as a general practitioner on Charles Street, sharing his office with Dr. James Sullivan Howe, one of the earlier Boston dermatologists. On Charles Street for some years many a young physician who afterward became locally famous began his practice. Whether through Dr. Howe's precept and example—because he was a man who inspired respect—or through a love for dermatology and syphilology, Morton Smith soon weaned himself from general practice and from then on devoted his life to cutaneous medicine. Contact at the Boston Dispensary in 1894 with Dr. Abner Post, a profound student of syphilis, must have narrowed his interest still more, so that thus early in his career Morton Smith gave all that was in him to follow worthily in his chief's footsteps—and he did not fail.

Such are the dry facts of this man's career, which was studded, as can be seen, with hard and successful work and the holding of high office.

When off duty—and that was not often or long—Morton Smith liked golf but better still his garden, where with his own hands he cultivated flowers and vegetables. Club life had few opportunities to flourish, but a quiet hour with friends at the Harvard Club of Boston gave pleasure and quiet relaxation.

The life of Morton Smith as a man and as a physician might well guide the younger medical generation in the path it should follow. He was sincere, honest, hard working, painstaking, modest and above all charitable. The patient and his story interested him as much as did the disease itself. The patient, in fact, came first in this man's mind.

Morton Smith did not come through life unscathed. In 1933 he was harassed by a duodenal ulcer, and in 1936 he suffered a mild cerebral hemorrhage. Then followed angina pectoris, and the final attack killed him at the end of twenty-four hours, on Jan. 8, 1938.

His world will miss this man.

CHARLES J. WHITE, M.D., Boston.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE IMPORTANCE OF STATISTICAL INVESTIGATIONS IN THE CAMPAIGN AGAINST CANCER. W. CRAMER, Am. J. Cancer **29**:1 (Jan.) 1937.

The chief value of statistics on mortality from cancer is in the information obtained about the remote causes of cancer, the proximate cause being, of course, unknown. Cancer is not a unit disease with a single etiology, and etiologic factors vary in different organs. Occupational cancer and social cancer are largely preventable. The term "social cancer" is applied by the author to cancer in which remote causes are to be found among the habits and conditions of life, and the incidence of this type of cancer, occurring in exposed sites, rapidly increases at the lower levels of the social scale. The inference is that the upper social classes have learned to avoid or remove certain remote causes of cancer in exposed sites. Statistical information is now available for approximately 200,000 annual deaths from cancer. Some of the conclusions drawn by the author are that the prevalence of the disease is not increasing, that cancer is not a disease peculiar to civilization, that the whole vertebrate kingdom is subject to it, that heredity plays only a predisposing rôle, that senility is not a determining factor, that cancer requires a long period of induction for its development and that the total incidence of cancer in different populations remains uniformly on a fairly even level.

THE PROGNOSTIC VALUE OF THE MITOSIS COUNT IN BIOPSIES OF LYMPHOSARCOMA. ALBERT E. CASEY, Am. J. Cancer **29**:47 (Jan.) 1937.

The author's study indicates that counts of mitoses may have a practical application in the study of malignant growths, particularly with reference to the prognosis. In studies of 125 cases in man the coefficient of mitosis in biopsy specimens was found to have a high correlation with the incidence of metastases and with the eventual mortality from the tumors. The primary tumor, the metastases and the recurrences were found to have the same mitotic coefficient. Malignant tumors showed more than four mitoses per thousand tumor cells and benign tumors less than four mitoses per thousand tumor cells, irrespective of type, site and mammalian species.

FOERSTER, Milwaukee.

CHANGES IN THE GROWING SKELETON AFTER THE ADMINISTRATION OF BISMUTH. JOHN CAFFEY, Am. J. Dis. Child. **53**:56 (Jan.) 1937.

Caffey selected four types of osseous lesions to illustrate the changes which follow bismuth therapy for syphilis. These were: (1) the lesion which occurs directly after a single course of treatment with a bismuth preparation; (2) that which occurs many weeks after a single course; (3) that which occurs after multiple courses during several years, and (4) that which occurs in the newly born infant whose mother received a bismuth preparation during pregnancy. Under the last heading are described the changes which take place (1) after a single course of treatment with a bismuth preparation late in pregnancy; (2) after a single course of treatment with a bismuth preparation relatively early in pregnancy, and (3) after two courses of a bismuth preparation during pregnancy.

All these observations have revealed shadows in the skeletal roentgenograms of such patients similar to the "lead lines" in lead poisoning. Similar changes were produced in growing dogs by the administration of bismuth preparations. The histologic features of the lesions are described. Chemical analyses of the bismuth zone with regard to the bismuth, the calcium and the phosphorus content are given.

CONGENITAL AND FAMILIAL ALOPECIA TOTALIS. JAMES B. GILLESPIE, Am. J. Dis. Child. **53**:132 (Jan.) 1937.

The author reports four cases of total alopecia in children whose parents were related. Three girls and one boy were affected. Four other children in the family had luxuriant hair. None of the children with total alopecia had any other ectodermal defect.

NELSON PAUL ANDERSON, Los Angeles.

SODIUM BISMUTHATE SOLUBLE. P. J. HANZLIK, A. J. LEHMAN and A. P. RICHARDSON, Am. J. Syph., Gonor. & Ven. Dis. **21**:1 (Jan.) 1937.

The authors have developed a new preparation of sodium bismuthate, called sodium bismuthate soluble [and later sobisminol], in solution and in dosage forms for intramuscular and oral administration in the treatment of syphilis. The details of preparation and the properties of the products are described. Extensive studies were carried out on the pharmacologic actions of the preparations. Alone, they are demonstrably effective on lesions of early and late syphilis when given intramuscularly or orally. The authors maintain that the results obtained justify an extended and controlled clinical trial.

REUTER, Milwaukee.

PATHOGENESIS OF ERYTHEMA NODOSUM (WITH SPECIAL REFERENCE TO TUBERCULOSIS, STREPTOCOCCIC INFECTION AND RHEUMATIC FEVER). WESLEY W. SPINK, Arch. Int. Med. **59**:65 (Jan.) 1937.

Spink critically studied 10 patients with erythema nodosum and reviewed the records of 133 patients observed at the Boston City Hospital during a ten year period.

As far as Spink could determine, in none of the 10 patients available for observation was there a causal relationship of erythema nodosum to tuberculosis. In 5 of the patients the eruption was preceded by a sore throat. In 3 there was a history of an "abscessed tooth" shortly before the eruption.

Bacteriologic and immunologic studies suggested a causal relationship with Streptococcus haemolyticus.

The analytic review of 133 cases showed a great preponderance of females to males (111 to 22), with the highest incidence in the third decade of life. The greatest number of cases occurred in the early spring. The curve of seasonal incidence closely approximated that of known streptococcic infections. Fifteen of the patients had rheumatic heart disease.

No significant relationship to tuberculosis was discovered, although a review of the literature left little doubt that erythema nodosum may be a manifestation of tuberculosis, especially in children. Other possible causes were discussed.

Spink concluded that erythema nodosum appears to be a nonspecific inflammatory reaction of the skin to a variety of bacterial, toxic and chemical agents.

ALLERGY (A REVIEW OF THE LITERATURE OF 1936). FRANCIS M. RACKEMANN, Arch. Int. Med. **59**:144 (Jan.) 1937.

After reviewing the year's advances in the general concepts of allergy, Rackemann discusses the various clinical phases. Under eczema he reviews articles on the medicolegal aspects and sensitization to ragweed, tulips, gasoline, adhesive plaster, clothing dyes and cod liver oil. He mentions the development of sensitivity as a result of cutaneous tests (Field and Sulzberger), and dermatitis resulting from sensitivity to fungi (Pennington) is reviewed.

Hopkins and Kesten are given credit for a useful discussion of urticaria (ARCH. DERMAT. & SYPH. **29**:358 [March] 1934).

Instances of hypersensitiveness to various drugs are enumerated and discussed briefly.

LYNCH, St. Paul.

EXPERIMENTAL STUDY OF CONGENITAL SYPHILIS, INCLUDING A STUDY OF THE INFECTIOUSNESS OF BLOOD, UTERUS AND PLACENTA OF PREGNANT RABBITS WITH EARLY SYPHILIS. JAROLD E. KEMP and PAUL D. ROSAHN, Bull. Johns Hopkins Hosp. **60**:45 (Jan.) 1937.

In a study of five pregnant rabbits with early syphilis, spirochetes were found in the blood and the uterus of the mother and in the placenta. However, no evidence of infection was found in 47 fetuses from 12 different mothers with early syphilis. It appears that either the placenta forms a barrier to the spread of the infection from the syphilitic mother rabbit to her offspring, or the spirochetes are destroyed after reaching the fetus. In addition, there was no difference in susceptibility to infection between the offspring of normal and of syphilitic mothers. No difference was noted in the development or viability of the two groups of young that could not have been explained by the limitations of the laboratory facilities for the breeding of animals.

NELSON PAUL ANDERSON, Los Angeles.

DOES THE GONADOTROPIC HORMONE INDUCE ANTIBODIES OR ANTIHORMONES? FELIX SULMAN, J. Exper. Med. **65**:1 (Jan.) 1937.

In 52 experiments on rabbits Sulman shows that the purified gonadotropic hormone has no antigenic function. The antihormones against the gonadotropic substances must accordingly be considered as protective ferments. Intensive treatment with gonadotropic substance freed from urine antigen should have no toxic or allergic secondary effects.

IMMUNOLOGICAL AND CHEMICAL INVESTIGATIONS OF VACCINE VIRUS. R. F. PARKER and C. V. SMYTHE, J. Exper. Med. **65**:109 (Jan.) 1937.

Parker and Smythe studied the metabolism of suspensions of elementary bodies of vaccinia and found no evidence of continued utilization of oxygen or release of acid. These findings support the view that viruses are inanimate substances rather than minute living organisms.

THE BACTERICIDAL PROPERTIES OF ULTRAVIOLET IRRADIATED LIPIDS OF THE SKIN. FRANKLIN A. STEVENS, J. Exper. Med. **65**:121 (Jan.) 1937.

Ultraviolet irradiation increases the content of active oxygen of the lipids of skin and of dried skin from which the lipids have not been extracted. The irradiated lipids of the skin are bactericidal, and emulsions of these lipids kill hemolytic streptococci promptly in comparison with emulsions of lipids which have not been irradiated.

The mechanism of this bactericidal action is probably similar to that with other fats and oils, the effect resulting from the active oxygen released on contact with the bacteria. The addition of neutralized cysteine hydrochloride to emulsions of normal or irradiated lipids reduces their bactericidal action, owing probably to the reducing action of the cysteine.

LYNCH, St. Paul.

COLLAPSE WHILE SWIMMING: THE MOST DANGEROUS CONSEQUENCE OF HYPERSENSITIVENESS TO COLD. B. T. HORTON and G. M. ROTH, Proc. Staff Meet., Mayo Clin. **12**:7 (Jan. 6) 1937.

Hypersensitiveness to cold may be manifested by symptoms of syncope while a person is swimming. Urticaria may occur. Immersion of the hands of a person sensitive to cold produces a drop in blood pressure, an increase in pulse rate and flushing of the face. These reactions suggest the release by cold of a histamin-like substance in the tissues.

Treatment consists in having the patient immerse the hands in water at 10 C. for one or two minutes twice a day for three or four weeks. A person may also

be desensitized to cold by subcutaneous injection of 0.1 mg. or less of histamine twice daily for two or three weeks.

MILLER, South Bend, Ind. [AM. J. DIS. CHILD.]

THE TREATMENT OF EARLY CARCINOMA OF THE LIP, WITH SPECIAL REFERENCE TO THE USE OF LOW KILOVOLTAGE X-RAYS. JOHN C. BELISARIO, M. J. Australia **1**:91 (Jan. 16) 1937.

The author regards roentgen irradiation in the treatment of early carcinoma of the lip as the method of choice. He does not deem it advisable to remove nonpalpable lymph glands and favors watchful waiting. In his series of cases there was subsequent glandular involvement in less than 1 per cent, and in none of them was there local recurrence. The following technic was employed: The lip is first everted, and then both sides of the lesion are irradiated, 700 units being used on each side. This treatment was used in seventy-two cases and subsequent glandular involvement was noted in only one case. The author recommends a peak voltage of 110 kilovolts, 6 milliamperes, a 2 mm. aluminum filter, and a skin-target distance of 10 inches (25 cm.). He favors a 2 mm. over a 1 mm. aluminum filter, as the local reaction and the temporary inconvenience are reduced. The technic of shielding is described. Results in fifty-eight cases in which treatment with either radium plaques or interstitial radiation was employed generally were in no way inferior to those obtained by roentgen irradiation. The interstitial irradiation proved much better than surface application.

The author favors roentgen over radium therapy for the following reasons: (1) shortness of time required for actual treatment (thirteen and one-half minutes for actual delivery of a dose); (2) absence of all pain; (3) elimination of the discomfort caused by the presence of implanted radium needles and their removal; (4) elimination of the necessity for preliminary attention to dental sepsis, and (5) a more localized, shorter and less distressing reaction than that following the implantation of radium needles.

BAER, Pittsburgh.

SCLEREMA NEONATORUM, LOCALIZED TYPE. MARIE KRESTIN, Proc. Roy. Soc. Med. **30**:412 (Feb.) 1937.

The case of a boy of 7 weeks is reported. There was a large indurated swelling over the heads of the right and the left great trochanter. The shoulders showed similar patches of thickening over the deltoids. The patches of thickening were in the subcutaneous tissue, were irregular and of symmetrical distribution in the body and were over bony prominences of joints. The overlying skin was not discolored, inflamed or tender.

WILLIAMSON, New Orleans. [AM. J. DIS. CHILD.]

HERPES ZOSTER AND THE CEREBROSPINAL FLUID. A. TOURAINE, Ann. de dermat. et syph. **6**:289 (April) 1935.

Data on the spinal fluid in 141 cases of herpes zoster (23 personally observed cases and 118 collected from the literature) are analyzed by Touraine. He found that meningitis accompanying zoster is frequent but variable. It would seem to constitute a secondary reaction, posterior to the nerve root and proportional in importance to the intensity of the cutaneous eruption. It is characterized essentially by lymphocytosis and increased albumin and sugar contents of the cerebrospinal fluid. In general, there is a parallelism between these three manifestations. The meningitis is silent, with no clinical manifestations. The age of the subject, the form of the eruption, its course and its anomalies (bilateral, generalized, etc.) do not seem to exercise any special influence on the spinal fluid. This reaction of the meninges is transient, disappearing in from fifteen to twenty days. It is prolonged only in cases in which there is persistent pain; it acquires, then, a certain prognostic value.

Evolutive Cycle of Demodex Folliculorum Hominis Viewed by Microphotography. Françoise Fuss, Ann. de dermat. et syph. **6**:326 (April) 1935.

The author has made a painstaking study of the evolution of Demodex folliculorum hominis by means of photomicrographs. The text of his article is well illustrated with cuts showing the various stages in the life cycle of this parasite. There are four periods in the life history, characterized by changes in form, in size and in interior organization and corresponding to the embryonic, the larval, the adult and the aged state.

Correlation of Lupus and Pulmonary Tuberculosis. E. Bruner and S. Wasowicz, Ann. de dermat. et syph. **6**:409 (May) 1935.

The authors studied one hundred and twenty cases of lupus vulgaris for evidences of pulmonary tuberculosis, with the following findings: In thirty-four cases there was a suspicion of pulmonary tuberculosis; in forty-three cases there were lesions, such as calcification of the pulmonary parenchyma, peribronchial sclerosis and pleural adhesions; in two cases there was doubtful tuberculous activity; in seven cases there was definite pulmonary tuberculosis, and in thirty-four cases there was no pulmonary involvement. It was found that among the patients without lupous lesions of the mucous membranes the incidence of pulmonary lesions was much lower than in those having them. From this study it appears evident that there is a definite relation between cutaneous and pulmonary tuberculosis, since the two coexisted in 60 per cent of the cases.

Mycosis Fungoides. J. Peyri, Ann. de dermat. et syph. **6**:481 (June) 1935.

Nine cases of mycosis fungoides are reported. Six of the patients died—four of the mycosis. The author was struck by the favorable effect of pyrexia on the disease. Two of the patients had typhoid fever, and one of these experienced complete disappearance of the mycotic cutaneous tumors. The patient later died of intestinal hemorrhage. Fever therapy was used in three other cases, with excellent, if only temporary, results, and the author praised it highly. He expressed the belief that some disturbance of the reticulo-endothelial system gives rise to the cutaneous lesions and that when irradiation is used it is better to treat the spleen, the liver and the bone marrow than the cutaneous lesions themselves.

Experimental Research on Cutaneous Tuberculosis and the Tuberculids. J. Gaté, P. J. Michel and P. Dugois, Ann. de dermat. et syph. **6**:510 (June) 1935.

Because of the well known fact that tubercle bacilli are extremely difficult to demonstrate in the lesions of cutaneous tuberculosis, either by direct examination or by inoculation of guinea pigs, these authors have for the past two years performed various experimental and serologic tests on a total of forty-three patients. Serial inoculations of blood into guinea pigs in twenty-one cases gave positive results in only three, but cultures of blood from all forty-three patients on Löwenstein's medium gave positive results in twenty-nine cases (67 per cent). The Arloing-Courmont serodiagnostic test gave positive results in twelve of thirteen cases in which it was used. The complement fixation test gave positive results in ten of thirty-three cases, and the Vernes resorcinol reaction was positive in eleven of twenty-five cases. The studies are to be continued.

Gandy, Houston, Texas.

Disappearance of Psoriasis at the Onset of Puberty. L. Spillman, P. L. Drouet and R. Weille, Bull. Soc. franç. de dermat. et syph. **44**:22 (Jan.) 1937.

A girl aged 12 years was first observed in December 1935, because of generalized resistant psoriasis and a body habitus suggestive of dystrophia adiposo-

genitalis. After a dozen treatments by short wave diathermy in the region of the hypophysis the psoriasis entirely disappeared. In the spring of 1936 the eruption reappeared and was influenced little by injections of anterior pituitary extract and vitamin C. At the beginning of September 1936 the menstrual period appeared for the first time, and within two weeks the psoriasis had entirely disappeared. The authors expressed the belief that endocrine factors rather than coincidence explained the phenomenon.

STOMATITIS DUE TO AVITAMINOSIS. A. SÉZARY and P. DE FONT-RÉAULX, Bull. Soc. franç. de dermat. et syph. **44**:64 (Jan.) 1937.

The authors discussed a case in which erosive stomatitis had resisted many forms of local treatment and had recurred over a year's time. The patient had been observed in five Parisian hospitals and had had temporary relief at the best. After careful questioning it was learned that for several weeks before the onset of the stomatitis the patient had lost his appetite and had been taking as food only potato purée and milk, omitting all solid foods, vegetables and fruits. The reason for the anorexia was not explained, although there seemed to be a definite psychopathic factor.

There were no signs of edema, purpura or subperiosteal hematoma (scurvy). The authors felt that the stomatitis was the sole manifestation of a vitamin deficiency, probably of vitamins C and B. The period of observation had not been long enough to prove their hypothesis definitely.

LAYMON, Minneapolis.

LEUKOPLAKIA ELECTROGALVANICA AND HYPERCHOLESTERICA: A CONTRIBUTION TO LEUKOPLAKIA IDIOPATHICA. KARL ULLMANN, Dermat. Wchnschr. **102**:381 (March 28); 425 (April 4) 1936.

Two relatively new forms of leukoplakia deserve special attention, namely, leukoplakia electrogalvanica and leukoplakia hypercholesterica. The first is usually accompanied with erosions and is definitely benign. In contrast, the second is apt to be more extensive and tends to recur. Both forms have been incorrectly considered postsyphilitic. In four of seven cases of leukoplakia hypercholesterica observed by the author, malignant degeneration occurred. Leukoplakia hypercholesterica is most often induced by mechanical or chemical irritation. In this form of leukoplakia, hypercholesteremia was shown to be present in the blood.

TAUSSIG, San Francisco.

TOBACCO AND CANCER. O. SCHÜRCH and A. WINTERSTEIN, Ztschr. f. Krebsforsch. **42**:76, 1935.

Tobacco tar was found to be free from polycyclic, aromatic hydrocarbons. Painting the skin and the mucous membranes of mice and rabbits with tobacco tar did not produce carcinoma, even in conjunction with mechanical or thermal irritation. Fractions of tobacco tar likewise had no cancerigenic action. With rabbits on a high cholesterol diet and treated previously with coal tar, warts and carcinoma could be produced by means of tobacco tar. It seems that tobacco tar can be a factor in cancer only when predisposition exists.

EGGERS, Omaha. [ARCH. PATH.]

SECRETION OF SWEAT IN CHILDREN. J. ADACHI, J. Orient. Med. (Abstr. Sect.) **25**:95 (Dec.) 1936.

Adachi conducted the following experimental observations in nine children ranging in age from 11 months to 6 years:

EXPERIMENT 1.—Regional Variations in the Amount of Perspiration: Twenty-two representative portions of the body surface were covered with small pieces

of blotting paper about 4 by 4 cm., each piece being covered with a corresponding celluloid dish in order to prevent evaporation. The subjects were placed in a warm room for ten minutes, and the weight of the paper before and after the experiment was determined in each case. In another series of experiments the amount of perspiration was determined by the discoloration method of Minor, the degree and intensity of staining being the index of secretion.

According to the results of these experiments, the forehead perspires most profusely, followed by the anterior and the posterior surface of the trunk; the amount of perspiration on the lateral surfaces and the extremities is remarkably low. The upper extremities perspire more than the lower, and on the former perspiration increases peripherally, while in the latter this relationship is reversed. These observations agree with those recorded by Ikeuchi and Kuno in adults.

EXPERIMENT 2.—Quantity of Perspiration: The difference in the body weight before and after ten minutes' stay in a hot chamber was measured by means of the Sauter balance. The amounts of perspiration, calculated per square meter of body surface, were compared in children and adults. The results showed no consistent difference between children and adults.

EXPERIMENT 3.—Active Sweat Glands: The number of active sweat glands per 0.16 sq. cm. of skin was determined by Jürgensen's method on different regions of the body in three children during the period of their most profuse sweating. The glands were found to be most numerous on the forehead, somewhat less numerous on the dorsum of the hand and least numerous on other portions of the extremities, so that the ratio of the number of sweat glands on the forehead to that on the extremities was 2:1. The regional distribution of perspiration seemed to correspond approximately to that of the sweat glands.

The anatomic observations revealed the number of active sweat glands per unit of cutaneous area to be much greater in children than in adults, and their density to be greatest in the extremities in children and least in the extremities in adults. These observations led to the conclusion that the amount of perspiration depends primarily on the number of actively functioning sweat glands. Since children are born with a full quota of sweat glands, the density of the glands becomes less and less as the cutaneous surface expands with growth. Not all sweat glands are in active function, but they may be activated according to the physiologic stimulus to meet the needs of any given situation for the maintenance of normal health.

KATO, Chicago. [AM. J. DIS. CHILD.]

PHYSIOLOGY AND PATHOLOGY OF SEBACEOUS SECRETION, PARTICULARLY IN SYPHILIS. S. SUZUKI, Jap. J. Dermat. & Urol. **40**:203 (Dec.) 1936.

The author investigated, according to the method of Schur and Goldfarb, the amount of sebaceous secretion in 113 normal persons, 90 patients with syphilis and 85 other patients. He arrived at the following conclusions:

The individual amount of sebaceous secretion depends particularly on sex and age. Until puberty it is somewhat less in males than in females, but after the onset of puberty the secretion in males is considerably higher. In adults the difference between the two sexes is marked except in the age period from 36 to 40. There is an increase in the amount of secretion in men in the age periods between 16 and 30 and between 46 and 50 and a decrease between 36 and 45. In women there are rises in the age period between 16 and 25 and between 36 and 50 and a decline between 26 and 35. In older persons there is a gradual diminution in the amount of secretion in both sexes, starting at the age of 51 years. In old men the amount of secretion is larger than in boys before the age of 15, and in old women it is less than in girls before the age of 16.

The graphic curve of these changes corresponds to the frequency curve of eczema and to that of its seasonal variations.

The sebaceous secretion in syphilis is increased in 79.5 per cent of untreated patients, particularly in those in the secondary stage, and it is decreased in 8.8 per

cent of cases. In treated patients there is an increase in 51 per cent, a decrease in 29.4 per cent and a subnormal amount in 19.6 per cent. In congenital syphilis the author found poor sebaceous secretion in five patients examined. The increased sebaceous secretion in syphilitic patients is distinctly diminished by administration of arsphenamine and bismuth. In healthy persons the amount of sebaceous secretion does not change after injection of arsphenamine and bismuth or sodium arsenate. In patients with comedones, seborrhea, seborrheic eczema, hyperhidrosis and alopecia areata there is almost always an increase in sebaceous secretion of from 28 to 240 per cent, compared to normal average values. In those with tuberculosis and diabetes mellitus there is always a diminution of from 50 to 85 per cent. In experimental rabbit syphilis sebaceous secretion has increased in 12 animals from 31 to 155 per cent in from four to twenty-two weeks after testicular inoculation.

In rabbits a rise in sebaceous secretion is produced by excessive amounts of fat and carbohydrate in the food administered during one or two weeks. The increase reached from 70 to 119 per cent by excessive administration of fat and from 11 to 38 per cent by excessive administration of carbohydrate. Continuation of this diet for more than two weeks not only does not increase the amount of secretion but, on the contrary, diminishes it.

INFLUENCE OF ECZEMATOUS CUTANEOUS CHANGES IN THE ACCUMULATION OF VITAL DYE IN THE LIVER, THE KIDNEY, THE SPLEEN AND THE INTESTINAL TRACT. N. TANAE, Jap. J. Dermat. & Urol. **40**:212 (Dec.) 1936.

Twenty-four rabbits in which dermatitis had been produced by croton oil were killed after they had been given intravenous injections of trypan blue. The liver, the kidney, the spleen, the intestinal tract and the testes were examined histologically, and the accumulation of the dye was compared with that in control animals.

The Kupffer cells and the histiocytes of the liver showed increased accumulation of dye, but the amount returned to normal after the disappearance of the dermatitis. The epithelial cells of the primary convoluted tubules of the kidneys showed a decreased accumulation of the dye during the acute stage of the dermatitis. In the early subacute stage the accumulation increased, and in the late subacute stage it reached normal. In the spleen there were at the beginning of the acute stage an increase in the number of the reticulum cells, which contained an increased amount of dye, numerous intensely stained histiocytes and general stasis in the tissue. These changes gradually diminished and disappeared in the early subacute stage of the dermatitis.

In the intestines the accumulation of the dye in the histiocytes diminished considerably in the acute stage of the cutaneous manifestation, disappeared in the early subacute stage and returned gradually to normal.

In the acute stage of dermatitis the accumulation of the dye in the different organs varied; in one it was increased and in another diminished. There were always poor staining of the nuclei of the parenchymal cells and increased stasis of all the organs.

The testes did not show any difference in the degree of accumulation of trypan blue from those of control animals.

CHROMOBLASTOMYCOSIS. Y. TAKAHASHI, Jap. J. Dermat. & Urol. **41**:31 (Jan.) 1937.

The author reports the case of a 50 year old peasant who for fifteen years had had an eruption which consisted of nodules and ulcers. In the pus round or oval double-contoured bodies varying in color from light to dark brown and in diameter from 5.5 to 9 microns were seen. The deeper part of the corium contained numerous nodules, which consisted of central abscesses, a middle zone of

epithelioid cells with giant cells and polymorphonuclear leukocytes and an outer zone formed by young connective tissue cells with hyperplastic fibroblasts, among which were numerous plasma cells, lymphocytes and polymorphonuclear leukocytes. Some of the vessels were occluded, owing to hypertrophy of the epithelium. Changes in the epidermis were secondary.

Fungi were abundant in the micro-abscesses and giant cells and occasionally in the lumens of the newly formed vessels. The fungi could be cultured easily on Sabouraud's dextrose-agar medium. The author puts this fungus provisionally into the group of Torula Persoon and calls it Torula poikilospora because of the multiformity of spores. Inoculation of human beings and animals with the culture material produced positive results. Thus, to the three species of fungi found in chromoblastomycosis, namely, Trichosporium Pedrosoi, Phialophera verrucosa and Hormiscium dermatitidis, the author adds a fourth one.

BLOOM, New York.

Society Transactions

NEW YORK DERMATOLOGICAL SOCIETY

PAUL E. BECHET, M.D., *President*

April 27, 1937

EUGENE F. TRAUB, M.D., *Secretary*

Papulonecrotic Tuberculid. Presented by DR. HOWARD FOX.

Mrs. A. S., aged 49, was previously presented before this society on Dec. 15, 1936 (ARCH. DERMAT. & SYPH. **36**:391 [Aug.] 1937). At that time she showed a profuse eruption of the face and, to a lesser extent, of the scalp. Opinions as to diagnosis were somewhat divided between some type of tuberculosis and acne varioliformis. About two weeks after the last presentation the eruption disappeared completely. A mild relapse occurred six weeks later, and the patient was again given intradermal injections of tuberculin, in dilutions of 1:1,000,000, 1:100,000 and 1:10,000. Both local and constitutional reactions followed, the patient being confined to bed for three days. Two weeks later the eruption again disappeared almost entirely. A second relapse occurred on March 25; intradermal injections of tuberculin in dilutions of 1:1,000,000, 1:100,000 and 1:10,000 were given. Improvement followed three days later. At the end of eleven days, however, the eruption flared up and assumed its present appearance. The patient now presents on the entire face a profuse eruption of highly inflammatory papules, some of which show umbilication. Only one pitted scar is visible. The menses are irregular at present.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I do not believe this condition is acne varioliformis, because I saw no scars. The final diagnosis is probably tuberculid. Tuberculid histologically sometimes does not show a tuberculoid structure.

DR. GEORGE M. MACKEE: I thought this condition was tuberculid at the last presentation, and I still think so, although I am uncertain of the type. Regarding the effect of the tuberculin treatment, my experience has been to get improvement only after months of treatment. If this condition were papulonecrotic tuberculid, I should expect pitted scars. The distribution of the lesions and the absence of scars are against both papulonecrotic tuberculid and acne varioliformis. My tentative diagnosis is tuberculid.

DR. EDWARD R. MALONEY: I should not call this condition acne varioliformis or papulonecrotic tuberculid. The clinical picture certainly is not that of papulonecrotic tuberculid. To me the eruption itself and the reaction to tuberculin, when used both as a test and as a treatment, would indicate the diagnosis of some form of tuberculosis, and in spite of the fact that the histologic examination does not show any real tuberculous tissue, I am inclined to believe this is some mild type of tuberculosis and not papulonecrotic tuberculid and certainly not acne varioliformis.

DR. EUGENE F. TRAUB: Is it usual for any form of tuberculid of the face to clear up suddenly, as this condition did, and then recur again and again? Is that not what might be expected of acne varioliformis? I should appreciate some information on that point as to whether this condition can be classed as papulonecrotic tuberculid or acnitis when the presenter makes such a strong point about the absence of the scarring which is so essential to all the diagnoses under consideration.

DR. H. H. WHITEHOUSE: I agree with the majority of the speakers. I think the condition is not acne varioliformis. For one thing, ammoniated mercury had no influence on it, and that medication would have influenced acne varioliformis. Besides, there are no variola-like scars.

DR. PAUL E. BECHET: I am inclined to the diagnosis of acne varioliformis of the acute, inflammatory type. The lesions are grouped and acutely red, and some of them, especially those on the forehead, have depressed centers. There are a few of them in the hairy area. The clinical picture, as a whole, in my opinion, fits that of acne varioliformis rather than papulonecrotic tuberculid.

DR. HOWARD FOX: The two diseases which must be differentiated are acne varioliformis and some type of tuberculid. The location of the lesions, the sex of the patient, the absence of scarring and the failure of the eruption to respond to ammoniated mercury all speak strongly against acne varioliformis. In my opinion, this condition is tuberculid of some type, though I am doubtful about the relation between the injections of tuberculin and the improvement which followed. As Dr. MacKee has said, the reaction may have been due to the action of a foreign protein.

Multiple Synovial Lesions. Presented by DR. J. FRANK FRASER.

S. R., a woman aged 48, presents multiple pea-sized nodules on the extensor surfaces of the carpal and the phalangeal joints. The duration of the oldest lesion is four years. The appearance suggests synovial lesions, but microscopic examination shows none of the pathologic features of that condition. All that the sections show is moderate hyperkeratosis, acanthosis and a mild, chronic inflammatory reaction in the upper portion of the corium. There is no suggestion of mucoid degeneration, such as is seen in synovial lesions.

DISCUSSION

DR. EDWARD R. MALONEY: I cannot see anything which looks like verruca clinically. The lesions are multiple and located around the joints and suggest to me lesions which are not necessarily synvoial but of the type seen in rheumatic arthritis.

DR. GEORGE M. MACKEE: I think this woman has several different lesions. She has on the left hand, in the proper place, one synovial lesion. I think the other nodosities are probably deposits of uric acid. She may have had a wart removed, which would explain the histologic picture.

DR. H. H. WHITEHOUSE: Clinically the picture conforms to that which years ago was called gouty tophi, but the patient states she has had no experience suggestive of arthritis.

DR. FRED WISE: I favor Dr. MacKee's interpretation. I think the patient has definite evidence of arthritis, and I should like the opinion of the members as to the diagnosis of rheumatic nodules, rather than any other diagnosis on two of the lesions. One lesion, as Dr. MacKee has said, is a synovial lesion, and the other two seem to me certainly not to be warts. There is no evidence of warts, and I do not see why the diagnosis of rheumatic nodules cannot be entertained.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I should not make a diagnosis of warts in this case, either clinically or histologically. I could not see any acanthosis in the section. This condition is probably due to some form of rheumatic disease, probably gout or some other type of rheumatic affliction.

DR. HOWARD FOX: In addition to ordinary osteo-arthritic changes, the patient presents an apparently typical synovial lesion. It is on the usual site for a synovial cyst, and it has attacked a middle-aged woman, as it does in most cases.

DR. J. FRANK FRASER: As all the members agree that the remaining growths show the typical clinical picture of synovial lesions, I shall request Dr. R. Emmet,

to whom this case belongs, to remove one of these for microscopic examination. I feel that Dr. MacKee's suggestion is the correct one, because it is in harmony with the findings of the pathologist, who made a histologic diagnosis of verruca.

Dermatitis Medicamentosa (Phenolphthalein). Presented by DR. J. FRANK FRASER.

E. W., a woman aged 22, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 3, 1937, with a scaling eruption of the lips of one week's duration. There were brown mottling of the abdomen and scaling of the palms. The condition completely cleared on April 17. On April 22 the patient was given one tablet of "ex-lax," which immediately caused a recurrence of the condition. On the following day some improvement was evident, but after ingestion of another "ex-lax" tablet, all the symptoms were promptly exaggerated.

The Wassermann and the Kahn test were negative.

DISCUSSION

(The members agreed unanimously with the diagnosis as presented.)

DR. PAUL E. BECHET: I should like to ask Dr. Buschke whether the consumption of phenolphthalein is as great abroad as it is in this country.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): The reason why phenolphthalein is given rarely in Germany is that most German physicians believe it causes colitis and inflammation of the kidneys. There is only one type of laxative used in Germany, a saline one which has no phenolphthalein in it. I have never seen a single eruption due to phenolphthalein.

Hemiatrophy with Atrophying Scleroderma. Presented by DR. FRED WISE.

S. M., a girl aged 14, has had brown pigmentation of the skin of the right side of the neck for the past ten years. The lobe of the right ear and the whole right side of the face have always been definitely smaller than the corresponding structures on the left side.

There are atrophy and pigmentation, with softening of the skin of the anterior half of the right side of the neck. On the upper portion of the affected area the skin is smooth and glistening, showing active evidence of scleroderma without any signs of thickening of the skin. The lobe of the right ear is shrunken to about one-sixth the size of the lobe of the left ear. The face is asymmetrical, owing to the smallness of the right half of the mandible and of the right maxilla as compared with the bones on the left side.

DISCUSSION

DR. HOWARD FOX: The patient presents an area of marked atrophy and some pigmentation. The condition may be the end-stage of morphea, though there is little to suggest that disease at the present time.

DR. JOSEPH J. ELLER: I should like to venture the diagnosis of a nevoid condition. The patient has had this condition since the age of 3 years, and it might have been there before that, without any pigmentation. The mother has at no time noticed any hardening of the skin. I wonder if this might be a nevus of some type.

DR. PAUL E. BECHET: If this eruption were located on the lower part of the leg in a middle-aged woman, it would be called acrodermatitis. It has the thinning and translucency of the skin seen in that disease.

DR. EUGENE F. TRAUB: I believe that Dr. Wise considered the possibility of nevus in this case. If only the pigmented patch were present, this might still be a possibility, but the atrophy and the loss of tissue of the lobe of the ear would seem to me to exclude any form of nevus, as I know of no type in which such a shrinkage of tissue would be part of the clinical picture.

DR. FRED WISE: Dr. Fox is right in questioning the designation of scleroderma in a lesion which is absolutely soft, and the diagnosis which Dr. Hopkins made of hemiatrophy is the correct one. This patient's jawbone is contracted on the affected side, and the lobe of the ear has shrunk without any preceding ulceration. Some of the French authors, particularly Gougerot, have described atrophy in which evidences of coexistent scleroderma can be seen with the naked eye. This patient shows such areas of scleroderma, but not in this light. Under the microscope there are the characteristic changes of scleroderma. Therefore, I think the condition is a peculiar type of hemiatrophy which belongs in the scleroderma group and which terminates in atrophy. I do not believe it is a nevus. It might be a "nevoid" disease.

A Case for Diagnosis (Cheilitis Exfoliativa? Lupus Erythematosus?). Presented by DR. J. FRANK FRASER.

M. S., a woman aged 38, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 1, 1937, with a scaling and crusting eruption on the lower lip of twelve years' duration. The patient states that she received ultraviolet and roentgen irradiation at different hospitals and received twenty-two injections of a preparation of a basic bismuth tartrate at a New York medical center, for lupus erythematosus. A recent histologic examination showed chronic dermatitis, without any of the microscopic features of lupus erythematosus. I favor the diagnosis of cheilitis.

DISCUSSION

DR. FRANK C. COMBES: I agree with the diagnosis of cheilitis rather than that of lupus erythematosus. There is no definite border at all to this lesion, whereas in lupus erythematosus of the lip the edge is pronounced just below the vermilion border. I do not think the lack of response to gold therapy would militate against lupus erythematosus. If the condition is cheilitis, there is a question in my mind as to its source.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I can make no positive diagnosis except cheilitis. A lesion of such long duration, if it were lupus erythematosus, would have led to atrophy by this time.

DR. GEORGE M. MACKEE: I think if this case were one of lupus erythematosus which had existed for so long a time the lip would be dry; the scales would be adherent, and, as Dr. Buschke says, there would be atrophy. I think the lupus would have involved some of the skin as well as the mucous membrane. On that basis I make a diagnosis of cheilitis exfoliativa.

DR. EUGENE F. TRAUB: I agree with what Dr. MacKee has said. In addition, my chief reason for classing this condition as exfoliative cheilitis is that the process is exudative. There is considerable serous discharge, which is covered by a large adherent crust. There seem to be no scales such as one would expect were this a case of lupus erythematosus.

Lipodystrophy Associated with Multiple Milia of the Face. Presented by DR. EUGENE F. TRAUB.

H. R., a woman aged 27, states that some type of eruption appeared on her face about eight months ago. The onset was marked by itching, and there developed what the patient considered to be mild eczema. She received treatment for a period of three months, consisting of internal medication, intramuscular and intravenous injections and various ointments. It was noticed that she was gradually losing subcutaneous fat on the face and that numerous little white dots were appearing on the skin. When first seen, the patient had an itching erythematous eruption on the face and edematous eyelids, and she seemed to be suffering from some type of contact dermatitis. She states that she has had attacks of this

type since infancy. When this eruption disappeared, the loss of subcutaneous fat of the face was definitely noticeable, as were many tiny milia scattered over the same area.

DISCUSSION

DR. FRED WISE: I should like Dr. Traub to state on what he bases the diagnosis and what the characteristic features of this disease are.

DR. EUGENE F. TRAUB: This case was presented for two reasons: first, that the disease is rare, and, second, that, so far as I know, no other case of this condition has been shown before this society. Since two such cases have just come under observation, I have had occasion to look up the rather scant literature on the subject. The disease is a progressive one, starting usually on the face and extending downward to involve the neck, the upper part of the trunk and the upper extremities but never extending below the buttocks, thus always sparing the lower extremities. The cause is unknown. It is presumed to be an endocrine disturbance of some kind. The disease manifests itself by a progressive loss of the subcutaneous fat, causing the shrunken appearance of the cheeks well illustrated by the present patient. Associated with this disease there is usually an assortment of dermatologic changes. In the present patient there are numerous milia, and she has suffered from seborrheic eczema off and on for a number of years. She states that she had eczema in infancy and a flare-up again in puberty. In the reported cases there has usually been an associated hypertrichosis or some pigmentary change. These changes were not present in this or in any other case in which there was in association simply severe acne. So far as I know, there is no relation between this condition and the various types of lipoidosis.

A Case for Diagnosis (Eczema? Lupus Erythematosus?). Presented by DR. EUGENE F. TRAUB.

A. L., a woman aged 30, states that the eruption observed on her face, on the dorsa of the hands and on her arms has been present practically continuously for seventeen years. Although the eruption has been subject to exacerbations and remissions, the patient says definitely that not even for as long as a week has she been entirely free from the eruption during these seventeen years.

On both cheeks and the nose there is an erythematous and vesicular eruption, the older lesions of which are crusted and show some scaling. On the face the eruption is in rather large patches. On the arms there are many discrete similar pea-sized vesicular and crusted lesions. The eruption has always seemed worse in the summer. The patient feels that she may be sensitive to roses, as she recalls that with the appearance of these flowers her eruption always seems to get worse. The itching is intense, and in some of the older areas thickening and lichenification are pronounced.

The Wassermann test was negative. Urinalysis showed no abnormality except a slight trace of albumin and a few pus and epithelial cells. The blood count showed 3,240,000 red blood cells, 92 per cent hemoglobin, 4,000 white blood cells, 53 per cent polymorphonuclear leukocytes, 39 per cent lymphocytes, 5 per cent eosinophils, 3 per cent monocytes and no basophils. A biopsy specimen was taken from one of the lesions on the arm and was reported as showing eczema. The histologic examination showed the epidermis to contain small vesicles. About the vesicles were round cells. Otherwise, with the exception of occasional perinuclear spaces, the epidermis was normal. There was moderate edema of the collagen fibers, associated with some granular degeneration, especially in the upper and the middle part of the corium, a profuse round cell infiltration and an edematous mesh.

DISCUSSION

DR. HOWARD FOX: The patient presents two different types of lesions, those on the face being typical of lupus erythematosus and those on the forearms presenting the appearance of an excoriated dermatitis. The lesions on the arms may

be part of the same process as that on the face, though such marked signs of itching are rare in lupus erythematosus.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): The changes on the face are those of lupus erythematosus. The lesions on the arms are just simple eczema. Some physicians think that lupus erythematosus is a disease of sensitivity to light, and this patient is probably sensitive to light. The eruption on the arms is probably caused by this sensitivity. I believe only one etiologic factor can be assumed in this case to have led to these two different types of outbreak.

DR. GEORGE M. MACKEE: I certainly should not care to be unequivocal in making a diagnosis here, but my inclination is to call this whole process lupus erythematosus of the disseminated type. The eruption is somewhat eczematized, but it is not exudative. It is dry. The scales are adherent, and the eruption is slightly violaceous, all of which fits in with what is ordinarily called lupus erythematosus. I agree that ordinarily lupus erythematosus does not produce itching, but I think all the members will agree that sometimes there is almost intolerable itching. I have observed cases in which the itching was the most distressing symptom.

DR. PAUL E. BECHET: I am inclined to think the whole picture is the same dermatosis, and I believe it is lupus erythematosus. There is no doubt that there are cases in which lupus erythematosus resembles eczema. The condition comes and goes and after a while remains permanently. As Dr. MacKee says, occasionally acute lupus erythematosus disseminatus will produce a great deal of burning and itching, particularly after exposure to the sun.

DR. EUGENE F. TRAUB: The patient clearly states that the disease has been present continuously for seventeen years, and although there have been slight remissions, she states that she has never been free for even a week in that entire period. Of course, I cannot vouch for the accuracy of this statement, because in the few times that I have seen her I have observed a marked change in the appearance of the eruption. Some observers even thought in the beginning that the condition might be erythema multiforme, because of the acuteness of the process at that time. Some eczematization has been present at all times. It is perhaps a little less noticeable today than usual. The condition is itchy, and the skin has been much scratched and is thickened. When examination is made in good daylight, there is considerable question as to whether there is any atrophy on the face, the bridge of the nose or elsewhere. If this eruption were lupus erythematosus of the face of seventeen years' duration, it would seem to me that atrophy would certainly be a definite feature. There seems to be little doubt that the condition is a toxic process in a patient who is sensitive to light. I am not certain how to designate it correctly, however.

A Case for Diagnosis (Papular Eruption on the Face, the Neck and the Chest). Presented by DR. EUGENE F. TRAUB.

S. C., a woman aged 30, presents a peculiar redness on the skin of the face of about two or three months' duration. Throughout the areas of redness are scattered what seem to be tiny yellowish brown nodules, almost suggesting apple-jelly nodules. On the neck and the upper part of the chest, without the presence of any inflammatory reaction, are scattered numerous tiny shiny flesh-colored papules. The eruption is practically asymptomatic, the patient seeking treatment simply because of the pronounced flush of the face. Permission to take a biopsy specimen was refused, and no other laboratory work has yet been done in this case.

DISCUSSION

DR. GEORGE M. MACKEE: I think the first diagnosis to be considered here by all means is dermatitis venenata. I remember that a number of years ago, when Lewandowsky's tuberculid first came under discussion, a diagnosis of derma-

titis venenata was usually made in conditions resembling this because of location, inflammation and the presence of papules and pustules. In a number of instances the condition turned out to be Lewandowsky's tuberculid. I think there is a possibility that this case may terminate as one of Lewandowsky's tuberculid but that dermatitis venenata must be excluded first.

DR. PAUL E. BECHET: I agree with Dr. MacKee that in this type of case dermatitis due to cosmetics must first be considered. The patient is the type of woman who might use them to excess, and it is perfectly plausible to suggest that cosmetics should be eliminated first.

DR. EUGENE F. TRAUB: I am sorry that the discussers did not consider the papular lesions found on the neck and the chest, which certainly are a part of this process. There is no inflammatory reaction about these lesions at all. They are discrete tiny noninflammatory flesh-colored papules. Whereas I can understand that the possibility of a dermatitis of external origin is reasonable when the patient is examined under artificial light, because of the redness of the face, certainly if all the lesions are considered together, such a diagnosis is not tenable. In fact, I do not know what form of dermatitis would cause a rather deep-seated yellowish papulonodule. I shall study the case from the standpoint of a possible rosacea-like tuberculid and will perform patch tests with a view to excluding any possible external irritation as a factor in this eruption.

Report on a Case for Diagnosis (Tuberculosis Cutis? Drug Eruption?). DR. EUGENE F. TRAUB.

G. G., a woman aged 47, was presented before this society in March 1937 (ARCH. DERMAT. & SYPH. **36**:1296 [Dec.] 1937).

The lesion on the leg has materially improved since the patient was presented last month. Seven doses of 5 grains (0.3 Gm.) of sodium chloride in enteric-coated capsules have been given by mouth at two hour intervals, and a wet dressing of sodium chloride was applied. She has had ultraviolet irradiation of the lesion on the leg. As the members may recall, this lesion disappeared once before when treated with local roentgen and ultraviolet radiation, unaccompanied with the use of sodium chloride. However, this prompt response definitely is against the diagnosis of tuberculosis cutis and speaks strongly for the diagnosis of a bromide or an iodide eruption.

Report on a Case of Lupus Erythematosus Disseminatus. DR. EUGENE F. TRAUB.

J. G., a man aged 26, was presented before this society in March 1937 (ARCH. DERMAT. & SYPH. **36**:1302 [Dec.] 1937).

About a week after the presentation a fever developed, the temperature rising to 101 F. There were some pains in the joints, and because of questionable rheumatic cardiac disease, the patient was hospitalized. He has now been thoroughly examined in the hospital, and the presence of rheumatic cardiovascular disease has been established. A focus of infection has been found in the ears, but it is doubtful if this chronic focus is the cause of the patient's present septicemia. Numerous white blood counts have been done, and the results of all have been rather low, ranging from 3,700 to 6,150. In all, about ten counts were made, the average being well below 4,500. Cultures of material from the throat showed two types of streptococci. Cultures of blood have repeatedly shown no abnormality. Hemolytic streptococci (95 per cent) have been isolated from the stools. The lupus erythematosus, while it has not spread much over the face or the arms, has appeared on the trunk in the form of numerous discrete persistent urticaria-like papules. The prognosis is definitely grave.

Report on a Case of Lesions on the Thumb. Dr. Eugene F. Traub.

L. L., a woman aged 32, previously presented, had three lesions on the right thumb which were thought to be warts. As a result of treatment with roentgen rays, two of these disappeared, but the larger one in the center of the ball of the thumb was still present when I examined her. The patient was forced to discontinue treatment because of intercurrent pneumonia, and as a result, I have not seen her within the last few weeks.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Frank C. Knowles, M.D., *Chairman*

Sept. 17, 1937

Thomas Butterworth, M.D., *Secretary*

Condylomata Acuminata. Presented by Dr. Reuben Friedman.

J. S., a white man aged 25, states that in April 1937 two "sores" developed on his penis. At the Los Angeles City Clinic examination of a smear showed no abnormality. A Wassermann test the same day gave "mildly positive" results. The patient received no treatment for ten days, after which another Wassermann test was reported as strongly positive. He then received two injections weekly, one of neoarsphenamine and one of a bismuth preparation, for the next twelve weeks. About one week after the last injection of bismuth (July 2, 1937) the patient noticed the appearance of small wartlike lesions around the anal orifice. These have continued to grow larger and more numerous and have recently become painful and itchy. At the Temple University Hospital on Sept. 1, 1937, the Kolmer, the Wassermann, the Kahn and the Kline test were negative. Since then the patient has received three injections of a bismuth preparation and two of neoarsphenamine, but there has been no local improvement. Grouped about and obscuring the anal orifice is a large cauliflower-like verrucous mass about 5 cm. in diameter. Fissuring and inflammation are present.

DISCUSSION

Dr. Thomas Butterworth, Reading, Pa.: Has he had a proctologic examination?

Dr. Reuben Friedman: No.

Dr. Robert L. Gilman: That these warts have appeared in spite of bismuth therapy is not surprising. I have been struck with the fact that such warts do not necessarily appear in areas or in patients subject to irritation or so-called filth and often occur in the type of patient who pays close attention to hygiene. It has been my experience that the condition is most refractory to treatment. I doubt if I should ever try a bismuth preparation in this type of case. In this case there seems to be a collection of anal warts which have appeared coincidently with the syphilitic infection.

Dr. Edward F. Corson: I agree with Dr. Gilman. I do not think there is any necessary connection between these warts and syphilis. Their appearance is more likely a coincidence.

Dr. Donald M. Pillsbury: How does Dr. Friedman propose to treat these warts?

Dr. Reuben Friedman: I shall treat them by electrodesiccation.

Dr. Donald M. Pillsbury: I had a similar case last year, and the lesions were thoroughly electrodesiccated. Later there was a mild recurrence, and roentgen therapy to a point possibly a little over the patient's tolerance was given.

I think it should be remembered when fairly long series of roentgen exposures are given that the rectal mucosa is considerably more sensitive to roentgen rays than is the skin, and such treatment has been shown recently by Ferguson to be a possible cause of bleeding. In the case I am discussing the warts recurred and were recoagulated, with successful results.

DR. MORRIS MARKOWITZ: I am partial to medication with mercurial preparations. I have a patient with condylomas around the anus who has been getting mercury protiodide for the last three weeks, and the warts are actually disappearing.

DR. REUBEN FRIEDMAN: In the first place, the unusual location suggests that the virus may have arrived here as a result of pederasty, which, however, the patient states that he has not practiced. The condition is interesting from another angle because of a superficial resemblance to condylomata lata occurring in a patient under treatment for syphilis. It is of further interest in view of the fact that bismuth has been suggested recently as a sure cure of warts. Here is an instance of a patient with venereal warts who has received, all told, some fifteen or sixteen injections of a bismuth preparation and in whom the appearance of the warts has not been inhibited. Evidently the bismuth had no prophylactic or curative value.

A Case for Diagnosis (Dermatitis Artefacta?). Presented by DR. CARROLL S. WRIGHT.

E. H., a Negro aged 26, is under treatment because of a strongly positive Wassermann reaction, receiving a bismuth preparation and neoarsphenamine alternately. Recently he has had an eruption on his hands which he states appears as "white spots" which become thickened and scaly. His answers to questions are evasive, but he appears eager to convince one of the presence of nonexistent lesions. On the posterior surfaces of the hands are numerous circular, sharply circumscribed depigmented patches. There are a few thickened scaling patches about 1 cm. in diameter. There are two superimposed, overlapping lesions on the dorsum of the left hand and a few on the nape of the neck. The Wassermann reaction was 4 plus. Scrapings showed no fungi.

DISCUSSION

DR. ABRAM STRAUSS: I suggest the possibility of an arsenical eruption of the more or less fixed type. The patient states that he had a number of injections before his lesions appeared. They remained during treatment. New lesions appeared when neoarsphenamine therapy was resumed.

DR. H. J. SMITH: I think the condition possibly factitial because the lesions heal rapidly if let alone. The patient says that the lesion he had on his hand was a raw surface two days ago.

DR. DONALD M. PILLSBURY: I should like to agree with Dr. Strauss' diagnosis of an arsenical eruption. At least, it seems worth while to give a test dose of an arsenical preparation and to determine by patch test whether there is sensitivity.

DR. ROBERT L. GILMAN: There is nothing extraordinary about the individual lesions, and the interesting point is that the lesions which are present, if they have been produced artificially, are mild and in no wise disabling. I believe that the consensus of the members is that they are noninflammatory. I agree with the diagnosis of drug eruption and believe the drug should be ferreted out.

DR. EDWARD F. CORSON: The lesions on the back of the neck do not differ markedly from those on the accessible parts.

DR. ABRAM STRAUSS: I believe that there is some distinction between so-called fixed arsenical eruptions of the white and of the colored race. If I remember rightly, I have observed several conditions of this exact type in Negroes which I was convinced were fixed arsenical eruptions. In the white race a fixed arsenical eruption does not assume so sharp an outline.

A Case for **Diagnosis (Exudative Discoid and Lichenoid Chronic Dermatosis).** Presented by DR. CARROLL S. WRIGHT.

H. H. G., a Jew aged 48, states that in January 1936 there developed an eruption, which gradually spread to involve the entire trunk, the extremities, the scalp and the face. Intravenous injections of sodium bromide, small doses (3 drops three times a day) of solution of potassium arsenite and application of Pusey's oil emulsion (containing liquefied phenol, oil of bergamot, powdered tragacanth, zinc oxide, prepared calamine and olive oil or liquid petrolatum) resulted in virtual clearing of the skin. Recently an entirely different type of eruption has developed. At present there is a papulosquamous eruption of nummular patches on the trunk. These are slightly infiltrated and virtually noninflammatory.

DISCUSSION

DR. HERMAN BEERMAN: Guided only by the appearance of the lesions I suggest the possibility of mycosis fungoides.

DR. H. J. SMITH: I think the condition is parapsoriasis.

DR. ROBERT L. GILMAN: Duhring's disease is my diagnosis.

DR. HOWARD EARLE TWINING: I am rather inclined to agree with Dr. Smith.

DR. DONALD M. PILLSBURY: I think a good part of the eruption would suggest lichen planus. There are a number of eroded lesions, which is somewhat against a diagnosis of lichen planus, but I feel that the man produces these himself on top of somewhat hypertrophied lichenoid lesions. Then, itching was intense at first, and there are undoubtedly large areas of typical umbilicated, shiny papules like lichen planus lesions.

DR. EDWARD F. CORSON: There is some wrong symptom for every diagnosis that has been made here. I prefer dermatitis herpetiformis.

DR. REUBEN FRIEDMAN: I wonder whether there is an added element of arsenical eruption. The patient has been getting solution of potassium arsenite for a year off and on. I believe Dr. Wright told me the patient felt better when he was taking the solution. When he was instructed to stop taking it he requested after a one or two week period that it be given to him again. It may be, therefore, that the picture is modified by arsenic.

DR. CARROLL S. WRIGHT: Having read the description of an "exudative discoid dermatitis" by M. B. Sulzberger and William Garbe in the ARCHIVES (ARCH. DERMAT. & SYPH. **36**:247 [Aug.] 1937), I feel that the condition in the case presented falls into that category. The patient here is a middle-aged Jew, a subject, according to Sulzberger and Garbe, with a predilection for the disease. According to the history, the eruption has apparently passed through an exudative and discoid phase and a lichenoid phase and at present is in the phase resembling the premycotic stage of mycosis fungoides.

Sarcoid of Boeck. Presented by DR. FREDERICK EARLE KUNKEL, West Hartford, Conn., for DR. JOHN H. STOKES.

M. P., a white woman aged 50, presents irregularly round and oval patches and plaques, rather sharply outlined, varying in size from 0.5 cm. to several times that and violaceous brown and brownish red, on the face, the thorax, the back, the buttocks and the upper and lower extremities. In many of the plaques can be felt small flat or slightly rounded nodules which are moderately hard and slightly sensitive. Diascopic pressure reveals a fair number of yellowish brown foci. A moderate number of the lesions show thin adherent scaling. Many show thin, parchment-like atrophic scarring with telangiectasis. The condition had its onset ten years ago on the face, the trunk and the extremities. The initial lesion was a violaceous plaque on the left side of the nose, which followed an attack of influenza. There have been three exacerbations, each in the spring, in 1932, in 1935, and in 1937. Each was accompanied by general malaise and lassitude. During the past two years the patient has had repeated attacks of flatulence, nausea and pain in

the upper part of the abdomen. There is lymphadenopathy of the cervical, axillary and inguinal lymph nodes. The liver and the spleen are easily palpable. The tonsils are hypertrophied and diseased. The patient is anergic to old tuberculin. Urinalysis showed no abnormality. The blood count showed 4,700,000 red cells, 5,000 white cells, 63 per cent polymorphonuclears, 19 per cent lymphocytes, 10 per cent monocytes and 8 per cent eosinophils. The Kolmer and the Kahn test were negative. Chemical analysis of the blood showed 22 mg. urea and 82 mg. sugar per hundred cubic centimeters. After hypodermic injection of phenolsulfonphthalein 55 per cent appeared in the urine in two hours. The sedimentation rate was 24 mm. in one hour. A smear of material from the nose showed no Hansen bacilli. Roentgen examination showed no abnormality of the gastro-intestinal tract, thickening of the mucous membrane lining the ethmoid and maxillary sinuses, a suggestion of a mediastinal tumor, clear pulmonary fields, a rather fine mottled appearance of the bones of the vault of the skull, normal bones in the hands and the legs, abnormal function of the gallbladder and an opaque gallstone. Histologic examination showed sarcoid of Boeck. A biopsy specimen taken July 5, 1932, in the Falk Clinic, University of Pittsburgh, revealed "a granuloma but not characteristic of tuberculosis." In July of this year a second biopsy was performed in the Falk Clinic, and the observations were interpreted as indicative of sarcoid. Treatment has consisted of tonsillectomy and two injections of bismuth subsalicylate intramuscularly. The lesions have improved 50 per cent.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: It is hard to make a diagnosis at this stage, although in some of the scarred areas one can feel an infiltration. The history of the elevated lesions and the microscopic picture give the diagnosis—sarcoid of Boeck.

DR. ABRAM STRAUSS: Some of those lesions when infiltrated may be diagnosed as sarcoid, but the picture tonight and the patient's history made me think of lupus erythematosus. She stated that the lesions began on her nose, and at that site there is a rather typical scar of a healed lesion of lupus erythematosus. On the leg there is a great deal of scarring. All the lesions are superficial, and I did not see any infiltrated areas that suggested sarcoid.

DR. DONALD M. PILLSBURY: I believe that the tonsillectomy was probably partly responsible for the improvement. The patient had received one dose of a bismuth preparation only a short time before. When she first came in, the features of both lupus erythematosus and sarcoid were prominent. Disseminating lupus erythematosus was strongly considered. The dermatosis was of long duration, and with each exacerbation there has been some malaise, not incapacitating but still present. I think that in a number of cases of sarcoid there have been shown some characteristics of lupus erythematosus. I recall one particularly in which there were lesions in the scalp which were suggestive of lupus erythematosus.

DR. HERMAN BEERMAN: I saw this patient for the first time tonight, and clinically I cannot say I should have made a diagnosis of sarcoid, but the histologic sections, which I saw earlier, showed sarcoid definitely. I was glad to notice that subsequently a report from Pittsburgh stated that the same diagnosis had been made there histologically.

DR. FREDERICK EARLE KUNKEL, West Hartford, Conn.: When the patient came in she had adenopathy of the cervical, the inguinal and the axillary glands. Roentgen examination revealed fine mottling of the skull, and the spleen was definitely palpable.

DR. ROBERT L. GILMAN: This is the type of case that deserves further study, because it apparently has features of both conditions. I was impressed by the lesions on the legs, which suggested some form of tuberculosis, not lupus erythematosus. When I saw the diagnosis on the sheet, I found myself in full accord. I think all the symptoms are compatible with it. Sections did not strike me as showing lupus erythematosus. The rapid involution is not attributable to bismuth alone.

MANHATTAN DERMATOLOGIC SOCIETY

ANDREW J. GILMOUR, M.D., *President*

Oct. 12, 1937

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Polycythaemia Vera. Presented by DR. GEORGE C. ANDREWS.

G. H., a man aged 45, was seen on May 6, 1937, at which time the face and the scalp were deep red and diffusely studded with papulopustules. The shoulders and a triangular area on the chest presented intense erythema, with multiple papules and pustules. The patient states that he has had polycythaemia vera for twelve years, the erythrocyte count varying from 7,000,000 to 13,000,000. The papulopustules first developed on the face six years ago and slowly spread over the scalp, the chest and the back.

Histologic examination of a papulopustule removed from the chest showed only a nonspecific inflammatory reaction about the hair follicle, with large numbers of polymorphonuclear leukocytes.

Treatment has consisted of the administration of roentgen radiation in doses of 100 r weekly to the face, the chest and the back for fourteen weeks. The scalp was treated similarly until temporary epilation precluded further exposures. Each week the patient was given 10 mg. of sodium gold thiosulfate intravenously.

The face is now clear. Moderate erythema persists. The chest and the back present only an occasional active lesion on a smooth skin, with some discoloration at the sites of previous lesions.

DISCUSSION

DR. HOWARD FOX: I did not know that any type of eruption was associated with polycythaemia vera. It would be necessary to observe a good many cases of this rare disease before any such relationship could be established.

DR. FRED WISE: Has this condition been treated in any other cases with gold solutions?

DR. DAVID L. SATENSTEIN: This patient has an eruption on the forehead, the face, the anterior part of the chest and the upper part of the back, the usual locations of acne. In this instance, since the condition of the patient is poor, acne could be a good deal aggravated. I cannot conceive on clinical grounds how the redness on the chest could be the result of the condition of the blood. This man has diffuse erythema, with a good deal of minute and multiple atrophy, which gives the impression of radiodermatitis or a sequela of irradiation. I think it is up to the presenter to prove that the condition is something special associated with the particular condition of the blood.

DR. FRED WISE: I should like to stress one point, namely, that there is no sign of radiodermatitis or atrophy in this condition.

DR. LUDWIG OULMANN: I observed a case of polycythaemia vera in a physician. I do not remember any cutaneous manifestation besides the flushed face, which is seen regularly. At autopsy in that case the internal organs showed some large areas of caseous tuberculous degeneration. Dr. Andrews stated that he obtained good results from sodium gold thiosulfate in this case. There is some scarring present which suggests tuberculosis. I should like to ask Dr. Andrews to make some tuberculin tests.

DR. GEORGE C. ANDREWS: Of course, it is hard to prove that the cutaneous lesions are due to polycythaemia vera. In that condition there is a plethoric appearance—a marked congestion resembling rosacea. This patient presented an extreme form of bluish red hyperemia, with pustulation and exudation. The scars resulted from the pustular and furuncular lesions. There was never any question of acne or any resemblance to it. At one time the erythrocyte count was 12,800,000,

but it is 7,000,000 at present. The patient was sick, and my associates and I considered him moribund. He had not been working for about six months, but he is now working. There is a marked improvement in his general condition.

There was an interval of about four months between the previous roentgen treatments (four fractional doses of 75 r) and our treatments. We continued with the fractional doses of roentgen rays and thought that perhaps a gold preparation in combination with the irradiation might be helpful. We figured that the patient's condition was toxic, and gold is supposed to neutralize toxic conditions. I am not sure which remedy to attribute the improvement to, but I suspect that it is due to the gold preparation.

Dr. Joseph Klauder has told me about a case of polycythaemia vera in which there was a widespread follicular papular eruption. He sent me some pictures of the eruption, which was distributed over the trunk and the extremities. Dr. Oscar Gans reported a deeply infiltrative cutaneous lesion in a case of polycythemia. Histologically it was composed chiefly of cells corresponding morphologically to small lymphocytes which gave a positive oxidase reaction.

Adenocarcinoma of the Breast. Presented by Dr. Ludwig Oulmann.

E. D., a woman aged 59, complains that an orange-sized tumor developed at the lower outer angle of the left breast, and ruptured shortly afterward, discharging pus and later serum.

The patient appeared two weeks ago at the clinic with a deep, badly smelling ulcer about the size of a large egg. It reached down to the fascia. The surrounding skin was infiltrated and inflamed. The clinical picture suggested gumma. The Wassermann reaction was negative.

Microscopic examination showed a fairly cellular malignant growth, the cells being arranged in solid alveoli with nests and ramifying columns and in some regions tending to form an acinar arrangement. The tumor cells showed dimensional variations but were usually of medium size. They were polyhedral, with granular, weakly staining basophilic cytoplasm and oval or round nuclei which varied in chromatic aspect and were sometimes reticular. In some areas the cells had undergone degeneration. The parenchyma in places predominated over the stroma, while in other places the reverse was true. The supporting connective tissue was either dense or loose, edematous and rather diffusely infiltrated with small round cells, plasma cells and relatively few polymorphonuclear leukocytes. A few scattered areas of myomatous degenerated cells were noted. The surface was ulcerated, and the tissue had undergone marked necrosis.

DISCUSSION

Dr. Isadore Rosen: I inspected the area around the nipple, and to me it looked as though the process might have had its origin in that location. I wonder if the condition is a type of carcinoma that began as Paget's disease.

Dr. J. Frank Fraser: In response to the question, I do not think this condition began as Paget's disease, which develops slowly and usually manifests itself around the nipple in the form of an eczematous dermatitis. The patient states that the duration of this lesion is only three months. Paget's disease would not produce so much damage in such a short period.

Dr. Anthony C. Cipollaro: Histologic examination showed definitely that this case is one of adenocarcinoma, and I believe that mastectomy should be done immediately.

Dr. David L. Satenstein: I wonder if the history given, that the growth is of three months' duration, can be taken seriously. This woman has a flabby breast and therefore may have had a small mass there for many years without discovering it.

Dr. Ludwig Oulmann: Histologic examination was performed last week, and it showed definitely that the condition is adenocarcinoma. There is no involvement of the lymph nodes, and therefore the prognosis is good.

Pigmentary Form of Verruca Plana. Presented by Dr. George M. Lewis.

R. B., a girl aged 17, states that small lesions developed on the chin three years ago. A number of flat-topped, irregularly shaped brownish elevations are scattered over the chin. Treatment during the past year has been with mild peeling lotions, mercury proto-iodide by mouth and injections of bismuth subsalicylate. Little if any improvement has resulted.

DISCUSSION

Dr. Fred Wise: There is no marked pigmentation in the lesions. However, I believe that this eruption corresponds to the ones described by Becker as verruca plana with pigmentation.

Dr. Isadore Rosen: What form of therapy has been employed? I suggest treating each one of the lesions with a mild desiccation spark. The result is usually good, and the treatment leaves no scars and produces little pain. I have obtained some good results with it.

Dr. David L. Satenstein: Besides the therapy suggested by Dr. Rosen, in a number of cases I have tried applying equal parts of glacial acetic acid and phenol after cleansing the skin thoroughly. The results have been good. The latter treatment dries the lesions up without producing any inflammatory reaction.

Dr. George M. Lewis: Pigmented flat warts are occasionally seen and, in common with ordinary warts, may prove resistant to ordinary therapeutic measures. Becker has recently described the characteristics of this type of wart (Becker, S. W.: The Pigmentary Form of Verruca Plana, Arch. Dermat. & Syph. **34**:265 [Aug.] 1936). I shall be glad to follow the therapeutic suggestions.

Lupus Miliaris Faciei. Presented by Dr. Anthony C. Cipollaro.

A. M., a housewife aged 60, entered the clinic on May 17, 1937, complaining of an eruption on the face of four months' duration.

The patient has several brownish red papular lesions on both cheeks. When diascopic pressure is applied, brown nodules are observed. These lesions are discrete and few. There is no suggestion of rosacea or a rosacea-like eruption. The patient has a scar the size of a 5 cent piece on the right side of the forehead. This scar is the result of treatment of a lesion which clinically resembled basal cell epithelioma. Two biopsy specimens removed from this lesion prior to destruction showed histologic characteristics of rosacea-like tuberculid of Lewandowsky.

Examination of the urine showed no abnormality. The Wassermann and the Kahn test of the blood were negative.

DISCUSSION

Dr. Howard Fox: The lesion which the presenter removed may have been lupus, but the two remaining small lesions on the cheek appear to be superficial basal cell epithelioma. At least they have unquestionably pearly borders.

Dr. David L. Satenstein: I should like to refer the members to a recent article by Sachs and Garbe in the Archives (Arch. Dermat. & Syph. **36**:273 [Aug.] 1937) on basal cell epithelioma, which called attention to the rolled or pearly border. This is not always present and is not characteristic of proved basal cell epithelioma. In an investigation of a large series of cases of supposed basal cell epithelioma, only four cases in which there was a pearly border turned out to be instances of basal cell epithelioma. In the other cases the condition proved to be something entirely different.

Dr. Anthony C. Cipollaro: The two lesions on the right cheek have a peculiar brownish red color, which in my opinion is characteristic of the tuberculids

in general. The lesions appear to be soft. The periphery of the lesions does not suggest to me the rolled pearly border so frequently diagnostic of epithelioma.

NOTE.—One of the lesions from the right cheek showed histologic features of lupus erythematosus.

Onychodystrophy. Presented by DR. ANTHONY C. CIPOLLARO.

L. S., a floor girl aged 25, came to the clinic on Aug. 14, 1936, with an eruption of the fingers of two years' duration.

The patient states that the involved areas were free from any cutaneous disease prior to development of the present condition. The condition involves the thumb and the middle finger of the left hand. The nails are yellowish, everted and thin and are attached only by the proximal portions. There is no subungual hyperkeratosis. The terminal portions of the thumb and the finger are smaller than normal. The skin is thin and shiny, and there appears to be loss of normal subcutaneous tissue. The condition of the nails improved during roentgen therapy but recurred soon after treatment was discontinued.

Several microscopic and cultural examinations for fungi gave negative results. The Wassermann and the Kahn test of the blood were negative. Chemical analysis of the blood showed a slight decrease in inorganic phosphate, there being 2.1 mg. per hundred cubic centimeters, and a slight increase in calcium, there being 11.5 mg. The basal metabolic rate was normal. The general physical examination showed no abnormality. The roentgenogram of the fingers of both hands showed a moderate degree of absorption of lime salts throughout more or less all the bones of the left hand. The atrophic condition was more discernible in the terminal tuft of the thumb or the middle finger of the left hand; in both of these fingers there was evidence of infiltration of the soft tissue on the dorsal aspect around the nails, suggesting paronychia.

DISCUSSION

DR. HOWARD FOX: I should like to know if there is any history of psoriasis in the family.

DR. DAVID L. SATENSTEIN: I should make a diagnosis of some type of fungous infection.

DR. LUDWIG OULMANN: If this condition should be a fungous infection, would not a culture or a microscopic test show it? In cases of dystrophy I obtained good results from the use of thyroid.

DR. GEORGE M. LEWIS: The clinical evidence favors the diagnosis of a fungous infection of the nails. The fact that only two nails are involved, the yellowish color and the large amount of dystrophy of the nails, which have become crumbly, all speak in favor of onychomycosis. One may have to make repeated examinations before fungi can be demonstrated. Failure to find fungi in one or two preparations should not be considered sufficient evidence to exclude fungous infection.

DR. ANTHONY C. CIPOLLARO: Whether there is a history of psoriasis in the family was not ascertained.

A Case for Diagnosis (Lymphangioma?). Presented by DR. LUDWIG OULMANN.

L. L., a woman aged 44, was seen at the clinic five days ago. The patient says that for the past three months she has had a tumor behind the right ear. This tumor is of the size of a bean now, is irregular and to the touch feels as though it reaches down to the cartilage. It consists of small semitranslucent yellowish brown elevations with small angiomas and capillaries between. The case is presented as one of possible lymphangioma. Liquid could not be obtained from the tiny blisters.

NOTE.—Histologic examination proved the lesion to be basal cell epithelioma.

DISCUSSION

DR. DAVID L. SATENSTEIN: I suggest a clinical diagnosis of basal cell epithelioma. This is not an uncommon picture. Around the lymph sinuses there is a basal cell neoplasm.

Neurotic Excoriations. Presented by DR. FRED WISE.

S. B., a married woman aged 34, is presented because of a pea-sized ulceration of two years' duration on the left cheek, about ¾ inch (2 cm.) lateral to the midportion of the nose. The patient states that she picks at the lesion with a pair of forceps. She is obsessed with the idea that something is present underneath the skin which produces irritation. What that something is is not clear to her. The ulcer has healthy-looking red granular borders, which slope toward the middle, since the trauma was effected in that direction. There is no discharge. The base and the surrounding tissues are soft and noninfiltrated. The regional glands are not palpable. In addition to the ulceration the patient presents numerous depressed healed, scarred areas of varying sizes and shapes on the chin, the forehead and the sides of the face. The earliest of these dates back eight years. The Wassermann reaction was negative.

DISCUSSION

DR. GEORGE C. ANDREWS: This patient was at the Vanderbilt Clinic about a year ago. The lesion at that time was larger than it is now. The diagnosis was dermatitis factitia.

DR. ISADORE ROSEN: It is interesting to see a patient with an ulceration that has been present for a few years and which although continually irritated does not show malignant changes. There must be some factor necessary for the development of malignancy besides prolonged irritation.

Pigmentation of the Eyelids (Lichen Planus?). Presented by DR. FRED WISE.

E. A., a girl aged 21, is presented because of a reticulated purplish brown circumorbital pigmentation of one year's duration. The pigmentation extends up to ¼ inch (0.6 cm.) below each eyebrow and down to the soft tissues of the lower lid and extends horizontally from the inner to the outer canthus. Physical examination and the Wassermann test have shown no abnormality. A lentil-sized spot of light brown pigment is present on the cornea of the left eye.

DISCUSSION

DR. HOWARD FOX: Dr. Michelson has recently reported a small series of cases (not yet published) in which he observed a reticulated pigmentation of the eyelids which proved to be lichen planus on microscopic examination. I should suggest the diagnosis of lichen planus in this case.

DR. DAVID L. SATENSTEIN: Sometimes it is almost impossible (under the microscope) to differentiate Riehl's melanosis from lichen planus with pigment. In this particular case I suggest the possibility of some connection between the pigment the patient is using on her nails and the pigment on her eyelids.

Oriental Sore Involving Brother and Sister. Presented by DR. MIHRAN B. PAROUNAGIAN.

H. T., a boy aged 8 years, and Z. T., a girl aged 11 years, of Armenian parents, were born in the United States. When the boy was 5 months old, the parents emigrated to Aleppo, Syria, and lived there until they left to come to America; they arrived in New York a week ago.

The duration of the boy's lesions is said to be nine or ten months. He has three lesions on the face, two being on the left side and one at the inner canthus of the

right eye, and one on the left leg. The upper lesion on the left side of the face appeared about ten months ago; the lower one, about one month later. The lesion at the inner canthus is said to be of two weeks' duration.

The upper lesion on the left side of the face is smaller than a dime, reddish and somewhat flattened, with a rough surface and an areola. The lower lesion is about the same size but considerably elevated. It is a hard nodule with a smooth surface and a red areola. The lesion of the inner canthus is more elongated and much flatter. The parents state that some pus was expressed during the voyage.

The lesion on the leg, which is of six weeks' duration, is a small, indolent ulcer, which the parents thought was caused by a splinter. Several small scars can be noted in the region of this ulcer.

The sister's lesion is situated on the bridge of the nose and extends in the direction of the inner canthus of the left eye. The lesion is crusted and irregular, and the duration is said to be eight months.

DISCUSSION

DR. HOWARD FOX: Active lesions of oriental sore are rarely seen in the United States. In a study of ten years' record J. M. Andrews was able to collect only ten cases which had been observed in the United States and Canada. Two of these were cases which I had observed at Ellis Island. In both patients the disease developed while they were on the way to America, and in the lesions of both of them Leishmania tropica was found with ease. Most of the photographs of this disease which I have seen have suggested impetigo or ecthyma. At times the lesions are numerous. One of my photographs shows ten lesions and another (From Beirut, Syria) fifty lesions of oriental sore. I am a little surprised that one of these children presents a fresh lesion, in view of the fact that she has several others of eight months' duration. Complete immunity is said to be established within one year, as the Arabian name *habel-seneh*, meaning button of one year, would indicate.

DR. D. L. SATENSTEIN: I saw sixty-three cases while I was away. The lesions at first are similar to those on this boy's face. They start as waxy granulomatous masses, later undergo degeneration and then present ulcerations; in the later stages, during the process of healing, they become crusted. The microscopic picture shows an ill defined granuloma. From the tissue alone one could not make a definite diagnosis.

DR. GEORGE C. ANDREWS: I believe the lupoid variety is common, and I think that the condition in these cases belongs in that category.

A Case for Diagnosis (Pityriasis Rubra Pilaris? Lichen Pilaris?). Presented by DR. FRED WISE.

J. M., a boy aged 15, born in the United States, consulted Dr. G. D. Astrachan. He stated that he had had an eruption for eight years. Recurrences took place every three or four years.

The patient presented a generalized eruption covering almost the entire body except the feet and parts of the hands and the scalp. It is composed of pinhead-sized elevated horny papules which are skin colored and conical. The skin has the feeling of a nutmeg grater. There is some scaling on the face. On the anterior aspect of both forearms there are several well defined, slightly elevated keratotic plaques. The dorsal aspects of the proximal phalanges of almost all the fingers are studded with tiny pinhead-sized lichenified, dark brown papules. The eruption is not accompanied with any subjective symptoms.

DISCUSSION

DR. HOWARD FOX: At the Bellevue Hospital the question of extensive keratosis pilaris or lichen pilaris in Negroes has recently been discussed. The condition appears to be much more common in the Negro than in the white man. As a rule

it has been impossible to ascribe this incidence to avitaminosis. It has been possible to exclude both lichen scrofulosus and pityriasis rubra pilaris. This case falls in the same nondescript category. I should certainly exclude pityriasis rubra pilaris, as the characteristic features of that disease are absent.

Alopecia Areata and Alopecia Cicatrisata. Presented by DR. ANTHONY C. CIPOLLARO.

P. R., a man aged 30, an investigator, came to the clinic on Sept. 24, 1937, complaining of loss of hair extending over six years.

The patient states that he never has had any eruption of the scalp. At present there are several bald areas scattered over the scalp. The skin in these areas is atrophic, thin and shiny. There is no evidence of folliculitis. The patient has several bald areas on the face, but in these areas the skin is not thin, shiny and atrophic. The loss of hair on the face started about two months ago.

The Wassermann and the Kahn test were negative.

DISCUSSION

(The diagnosis was unanimously accepted.)

A Case for Diagnosis (Psoriasis Arthropathica? Osteitis Cystica Tuberculosa [Jüngling]?). Presented by DR. GEORGE M. LEWIS.

F. V., a man aged 27, states that an enlargement of the distal portion of the left index finger developed eighteen months ago. The thumb and two other fingers of the left hand and the index and the fourth finger of the right hand became similarly affected. The swellings were chiefly in the terminal interphalangeal joints of those fingers and were painless, but movement of the fingers was difficult. Both great toes were said to have been involved but had healed spontaneously. An audible cracking was noted when the fingers were moved. Several nails showed vertical cracks and dystrophic changes. When the condition began there were numerous lesions of psoriasis on the exterior portions of the arms and elsewhere. Roentgenograms revealed changes supposedly characteristic of osteitis cystica tuberculosa. There was evidence of healed tuberculosis in the roentgenogram of the chest. The tuberculin test and the Wassermann test gave negative results. The tonsils were markedly enlarged and cryptic.

DISCUSSION

DR. GEORGE C. ANDREWS: The diagnosis has to rest largely on the roentgenographic evidence.

DR. FRED WISE: Did the roentgenogram of the skeletal system reveal any cystic changes in the long bones of the extremities?

DR. ISADORE ROSEN: Time and again patients with lesions of sarcoid are referred for thorough investigation for a tuberculous focus. In most cases the results are negative.

DR. MIHRAN B. PAROUNAGIAN: This patient states that a similar condition on his toes healed. These diseases of the joints remind me of the lectures of the late Dr. Piffard, who used to mention rheumatism among the possible causes of psoriasis. I should be more inclined to accept such a diagnosis than one of sarcoid.

DR. GEORGE M. LEWIS: An article by Jeghers and Robinson on psoriasis arthropathica recently appeared in *The Journal of the American Medical Association* (**108**:949 [March 20] 1937). The authors pointed out that the changes in the joints are not characteristic roentgenologically. In other words, destructive and other types of arthritic changes appear in different cases, so that one cannot determine by roentgen examination whether the condition is psoriasis arthropathica.

Granuloma Annulare. Presented by DR. GEORGE M. LEWIS.

BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *President*

Oct. 28, 1937

HENRY SILVER, M.D., *Secretary*

Disseminated Xanthomatosis. Presented by DR. LEO SPIEGEL.

J. S., a man aged 67, a native of England but a resident of the United States for the past thirty-nine years, came to the clinic of the Lenox Hill Hospital on Oct. 26, 1937. His eruption is of two years' duration and involves the entire face and neck, all the flexural surfaces (axillary, cubital, inguinal and popliteal) and the mucous membranes of the mouth. The lesions are discrete macules and papules, which vary in size from that of a pinhead to that of a pea or slightly larger and form small plaques in some areas. The macular lesions vary from dark red to purple, and the elevated papules and nodules are characteristic yellowish red and yellow. The lesions on the eyelids are numerous and interfere mechanically with the opening and closing of the eyelids. The patient complains of intense itching, although there is no evidence of scratch marks.

DISCUSSION

DR. FRANK E. CROSS: A point of great interest is the distribution. Usually xanthoma appears on the extensor surfaces of the extremities, over areas of pressure. The color corresponds to the diabetic type of xanthomatosis, although this patient apparently is not suffering from diabetes.

DR. ARTHUR SAYER: Judging from the lesions present on the face, I should say that there is a tendency to spontaneous involution. The patient stated that the lesions appeared first on the face and were moderately elevated. Now they seem to have flattened down. The lesions on the other parts of the body are definitely raised.

DR. CHARLES WOLF: A clinical feature which is unusual and is pronounced in this case is the vascular appearance of some of the lesions. This would indicate that a histologic examination might show hemangiofibroxanthoma.

DR. LEO SPIEGEL: The rather unusual clinical picture in this case is in contradistinction to that seen in the tuberous variety of the disease. According to Montgomery, who reported 113 cases, the tuberous and the disseminated variety are similar histologically. The lesions begin as red macules, and as evolution takes place one can see the yellow deposits of lipoids. This patient complains of intense itching, but there seems to be no objective evidence of this. He was originally seen in the ocular department of the hospital because of the mechanical inability to open and close the eyelids. The urine was examined with Benedict's solution, and no sugar was found.

Atrophic Areas of the Subcutaneous Layer of Fat in a Patient with Friedreich's Ataxia and Diabetes Mellitus Treated with Injections of Insulin. Presented by DR. WILHELM FREI (by invitation).

This patient, a woman aged 21, from the Montefiore Hospital for Chronic Diseases, has suffered from Friedreich's ataxia for the past fifteen years and from diabetes for about six years, during which time she has been receiving insulin.

The patient states that more than a year ago depressed areas in the skin first appeared on the inner aspect of the right thigh, and later similar areas appeared on the left thigh. About seven months ago an area developed on the lower outer part and another area on the upper inner part of the upper portion of the right arm. The patient has not received injections of insulin in the depressed areas on the thighs, but probably the areas of the arm have been the sites of injection. These areas have never shown any signs of inflammation.

The areas involved are depressions varying in size from that of a 25 cent piece to that of a silver dollar and are produced by a deficiency of the subcutaneous layer of fat. The overlying skin can be lifted more easily than the skin in the unaffected parts. The areas on the inside of the thigh (Scarpa's triangle) are not sharply circumscribed and are connected with each other. The area on the lower part of the arm is well defined; the one on the upper part of the arm is just developing.

There are three possible explanations for the development of the fat atrophy: 1. It could have been produced by the insulin. There are a few cases recorded in the literature in which atrophy caused by insulin has occurred not only in the sites of injections but in other areas. 2. It could be connected with Friedreich's ataxia. The skin, however, participates only to a low degree in the atrophic changes of Friedreich's disease. 3. It could have been produced by the combination of injections of insulin and nervous disturbances.

DISCUSSION

DR. WILHELM FREI (by invitation): These lesions begin either with atrophy or with swelling. It is of special interest that the atrophy is not limited to the sites of injections, which is unusual, but appears in untreated areas of the body as well. I have found in the literature one such case, recorded in 1930 by Strunsky, who cited another case. I have mentioned three possibilities with regard to the development of the fat atrophy. I should like to point out that such atrophy occurs after drugs other than insulin—for instance from injections of pituitary extract—when they are given repeatedly in the same areas.

Grouped Pigmented Spots Following Injections of Insulin. Presented by DR. WILHELM FREI (by invitation).

This patient, a woman aged 67, from the Montefiore Hospital for Chronic Diseases, has had lupus vulgaris on the upper part of the right arm for thirty-five years, diabetes for nine years and pulmonary tuberculosis for six years. She has been given injections of insulin by her daughter, who boils the syringe and the needle before each injection. For the first three years there were no disturbances of the skin at the sites of injection, but for the past three years (of the six year period of the administration of insulin) inflammatory papules with slight suppuration have frequently occurred and been followed by pigmentation and sometimes by superficial scarring. During the patient's stay at the hospital (since the beginning of this month) no inflammatory changes following the injections of insulin were observed.

The picture is extraordinary. From thirty to one hundred brown spots the size of a lentil are grouped in relatively small areas on the upper parts of both arms and on both thighs. The brown coloring looks like melanin. On some sites, especially on the thighs, one can still recognize the inflammatory origin of these spots. Many of them show superficial scarring.

This picture seems to be similar to that noticed in drug addicts after injections performed under insanitary conditions. Why the inflammation and pigmentation appeared after the use of insulin for three years is not known. According to the patient's own story, her condition has not become worse during the last three years, but her statements are not exact. The condition is not due to acquired sensitivity to insulin, since the patient is now receiving insulin without any cutaneous reaction.

There is another patient at the hospital with diabetes and pulmonary tuberculosis who also presents brown spots after injections of insulin.

DISCUSSION

DR. PAUL GROSS: This patient has lupus vulgaris. The lesions produced by the injections of insulin are rather solid papules with necrotic centers, which after healing leave small round, depressed scars and pigmentation. In other words, these lesions clinically conform to the picture of papulonecrotic tuberculid. Such reactions have been seen in patients who are allergic to tuberculin after injections not only of tuberculin but of other drugs. I do not believe contamination has played any part in producing the reaction in this case.

DR. CHARLES LERNER: I wish to suggest an explanation different from that of the previous speaker. The pigmented spots are apt to be caused by particles of dust and desquamated epidermal cells introduced into the skin by the point of the needle and thereby producing more or less multiple traumatic tattoos. An addict or any patient, although he knows the importance of a sterile needle, scarcely ever bothers to sterilize or even to wash the skin prior to giving himself a hypodermic injection.

DR. LOUIS CHARGIN: Those who have had occasion to observe morphine or cocaine addicts will recall the so-called blue atrophy of the skin, which is identical with the process seen in this patient, except for the bluish color seen in addicts. This atrophy occurs regardless of whether the patients have tuberculosis or not. I do not think that one can attribute the atrophy to the tuberculous process of this patient, as Dr. Gross' interesting remarks imply.

DR. WILHELM FREI (by invitation): This patient has been giving herself injections of insulin and has boiled the syringe and cleaned the site of the injection with alcohol at all times. She has been taking injections for the past six years. During the first three years no changes occurred; during the second three years the present condition developed. The patient has tuberculosis, which has progressed. It is possible that there has been a change in the tissue due to the tuberculous process. In another patient suffering from tuberculosis and diabetes and taking injections of insulin, similar spots developed when the tuberculous process became more active.

A Case for Diagnosis (Folliculitis Sycosiformis Atrophicans) in a Syphilitic Patient. Presented by DR. HENRY SILVER.

U. S., an Italian aged 56, a tile worker, is a patient at the clinic of the Mount Sinai Hospital. He was treated in 1934 for swollen testicles and in 1935 for an ulcer of the tongue. He has not received antisyphilitic treatment.

An eruption appeared about four weeks ago and is strictly limited to the hair line of the temporal and the frontal part of the scalp; it is associated with loss of hair. The skin in an area ¼ inch (0.6 cm.) wide is dark red and densely set with pustules. On the forehead at the hair border there is wrinkling and slight atrophy.

The Wassermann reaction was 4 plus. The patient was given five injections of bismuth subsalicylate and no local therapy. There was slight improvement of the eruption.

The histologic examination showed changes suggestive of syphilis.

DISCUSSION

DR. ARTHUR SAYER: Did this patient receive intravenous injections of arsphenamine? I do not believe that one can justly eliminate the diagnosis of syphilis on account of the mild antisyphilitic therapy thus far given, namely, five intramuscular injections of bismuth. If there is a strong suspicion that this eruption is syphilitic, then certainly two or three injections of arsphenamine should be given and the effect on the suspected eruption observed.

DR. FRANK E. CROSS: I had occasion to see this patient two weeks ago, and I considered the eruption as tertiary syphilis. I was surprised this evening not to see more improvement from the treatment so far administered. I do feel, however, that one should not rule out a tertiary syphilitic eruption because the improvement was so slight. I suggest giving this patient mixed treatment by mouth.

DR. WILBERT SACHS: I do not think that this condition is folliculitis in the ordinary sense of the word, since there is no necrosis and no abscess formation. Acne varioliformis too can be ruled out.

DR. G. D. ASTRACHAN: I cannot make up my mind whether the eruption is folliculitis sycosiformis atrophicans or folliculitis decalvans, but I believe that the systemic syphilitic infection might have influenced the clinical aspect of the

present eruption. There are recorded cases of a condition called syphiloid, which is a nonsyphilitic cutaneous eruption resembling syphilis (Glaubersohn, S. A.: La syphiloïde papuleuse post-impétigineuse, *Acta dermat.-venereol.* **15**:77 [March] 1934).

DR. LOUIS CHARGIN: A patient who presents active manifestations of late secondary or tertiary syphilis and who has never had any treatment usually responds most rapidly not alone to mixed treatment but to any form of antisyphilitic treatment, such as injection or inunction of mercury preparations, and even administration of mercury protiodide pills or arsphenamine. If this eruption were syphilis it would have melted away under the treatment given. In a patient who has previously had antisyphilitic treatment the response to treatment may not be so prompt. In my opinion the eruption can hardly be regarded as serpiginous. While it is true that in late syphilis the lesions tend to form segments of circles, they do not follow the borders of the hair line as strictly as in this case. However, further treatment should be given, and if there is no response in a short time a syphilitic eruption can be ruled out. I still think that the eruption is not syphilis, although I fully realize that almost anything can happen in syphilis.

DR. PAUL GROSS: It seems to me that on the forehead there is atrophy marking the healed part of a serpiginous lesion. Without that assumption neither the diagnosis of serpiginous syphiloderm or that of folliculitis sycosiformis atrophicans can be maintained, and acne varioliformis confined to the frontal hair line should be considered. But if this condition is really a serpiginous lesion, the demarcation at the hair line is in favor of tertiary syphilis, which in my experience is more likely to stop at the hair line, while atrophic sycosis would spread to the hairy scalp. I favor the diagnosis of syphilis.

DR. THEODORE ROSENTHAL: I am reluctant to disagree with Dr. Chargin on a diagnosis of syphilis. However, I think that this eruption is syphilis, and my opinion is based on histologic and clinical grounds and the therapeutic response. It seems that the eruption is made up of three segments of circles, following strictly the hairy border. Histologically there is a tremendous infiltration of plasma cells; certainly one does not see that type of pathologic change in folliculitis. One does, however, see that change in syphilis. As far as therapy is concerned, I recently had occasion to inquire about the drugs used in the treatment of syphilis and found that there is a great difference in drugs bearing the same labels. Perhaps the injections of bismuth subsalicylate that this patient received did not contain enough bismuth to influence the condition.

DR. ARTHUR SAYER: Nobody can seriously argue about the rapid effects of the therapeutic test in syphilitic patients who have never been treated before, but occasionally one has an unusual experience. Recently I had a patient who presented the clinical manifestations of late secondary syphilis and a 4 plus Wassermann reaction. The response to the usual antisyphilitic treatment was insignificant for over two months; yet the eruption yielded to further therapy. Therefore, I must repeat that the treatment that the presented patient received is as yet inadequate to justify forming a definite opinion.

DR. HENRY SILVER: The difference of opinion expressed this evening, whether the eruption is syphilis or a sycosiform eruption in a syphilitic patient, was voiced at another meeting. It was decided not to use any local therapy and to institute antisyphilitic treatment. Up to date the patient has received five injections of bismuth subsalicylate, but the response has been slow. So far, the therapeutic test has failed. Dr. Samuel Peck, who studied the histologic sections, reported marked infiltration of plasma cells around the vessels and changes of the vessels suggestive of syphilis. Antisyphilitic treatment will be continued.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. MAX BERKOVSKY.

S. R., a man aged 61, a presser, is a patient at the clinic of the Bronx Hospital. He states that he noticed an oval lesion on the right temple two months ago.

Shortly afterward there developed several other lesions, involving the right temple, the right cheek, the right groin, the left axilla and the back. The patient has not lost any weight. He states that he has not taken drugs or iodized salts and does not take cathartics. A biopsy was performed at another clinic.

The lesions are isolated and bluish, vary in size from that of a small pea to that of a 25 cent piece and are situated on the right temporal region, the right cheek, the back, the left axilla and the right groin. The lesions on the temple are slightly depressed and mildly pruriginous. The lesion in the left groin is the size of a walnut, is fungating and has an uneven surface. There is involvement of the buccal mucosa.

The Wassermann reaction was negative. The examination of the blood, including a differential count, showed no abnormality.

DISCUSSION

DR. WILBERT SACHS: The microscopic examination showed granulation tissue in the subepidermal region and suggested an impetiginous lesion. There was no evidence of a drug eruption. There were a few features suggestive of an early prickle cell epithelioma, which diagnosis I do not favor. I believe that the tissue sent for microscopic examination differs from the other lesions present this evening. One physician who examined the slides suggested pemphigus vegetans.

DR. ADOLPH ROSTENBERG: The infiltrated tumor in the groin and the other lesions give me the impression of lymphoblastoma, in spite of the negative results of tests of the blood. I am inclined to this diagnosis because of a similar case which I presented two years ago before this society.

DR. CHARLES WOLF: A diagnosis cannot be made without the aid of laboratory methods. My tentative diagnosis is myelogenous leukemia in the aleukemic stage.

DR. PAUL GROSS: The combination of inflammatory and exudative lesions on the forehead and the trunk with flat tumors in the groin and the axilla is one factor in favor of the diagnosis of pemphigus vegetans. I feel this diagnosis should not be discarded until lymphoblastoma of the skin has been proved histologically.

DR. HENRY SILVER: One must stress the fact that no two lesions in this patient are alike. The lesions on the forehead are flat, round and bluish; the lesion in the groin is a massive fungating lesion; the lesion on the back is crusted. Tiny lesions on the face could suggest pigmented moles and the axillary lesion a melanoma. The laboratory data were of little help, and the histologic study must be considered inconclusive. The histologic diagnosis made on the basis of study of one lesion on the back cannot be accepted as a diagnosis for the varied clinical picture.

A Case for Diagnosis (Acrocyanosis with Xanthoma-like Nodules of the Elbows?). Presented by DR. MAURICE UMANSKY.

S. L., a married woman aged 31, presents a cutaneous disease which appeared about June 1937. She states that the upper extremities are sensitive to cold; she suffers from chilblains in the winter. The personal and the family history are irrelevant. She has a healthy child, 18 months old.

The skin over the elbow has a normal appearance when the forearm is extended. When the elbow is bent, a group of yellow nodules the size of a lentil or a pea can be seen and felt around the olecranon. They are not raised above the surface of the skin. A bluish area is present around the elbow and extends down to the middle of the forearm. The fingers of both hands are slightly swollen and cyanotic. When the fingers are flexed yellow deposits are visible around some of the articulations.

The examination of the urine showed no glycosuria. The sugar content of the blood was normal. The cholesterol content was 266 mg. per hundred cubic centimeters of blood. Permission for a biopsy was refused.

DISCUSSION

DR. PAUL GROSS: If these lesions showed sufficient atrophy, one could understand the formation of such nodules as seen in the late stages of acrodermatitis chronica atrophicans and consider them fibrotic nodules with deposits of cholesterol. Since this diagnosis can be eliminated on clinical grounds, I see only one other possibility. The lesions present in this patient are circumscribed bluish red plaques with a glistening surface and telangiectasis and show lemon-yellow infiltration in their center, especially on pressure. Such a clinical picture suggests the diagnosis of necrobiosis lipoidica. The only objection to this diagnosis is the absence of diabetes, but this objection I can easily overrule by the experience (to be published shortly) that the disease described by Urbach is not always associated with diabetes. A biopsy will likely clarify the diagnosis.

DR. HENRY SILVER: I have seen this patient elsewhere, and I am surprised that a diagnosis of acrodermatitis chronica atrophicans was seriously considered. One should not confuse the yellowish nodules of this patient with the fibrotic nodules and bands described by Oppenheim as late manifestations (*Ausgänge*) of the disease. The duration of this eruption is only approximately five months, and on that basis alone, aside from the clinical appearance, acrodermatitis chronica atrophicans can be ruled out. The resemblance to acrodermatitis chronica atrophicans, however, will strengthen Dr. Gross' diagnosis of necrobiosis lipoidica (Urbach). It will be remembered that the first cases were recorded by Oppenheim under the name of dermatitis atrophicans lipoides diabetica.

DR. MAURICE UMANSKY: The diagnosis of incipient acrodermatitis chronica atrophicans associated with cutaneous nodules can hardly be considered in this case. There is complete absence of atrophy and scaling. Tumefaction of the skin, which is present in the early stages of dermatitis atrophicans, is missing in this case. Juxta-articular nodes are not to be thought of as a likely diagnosis. Those are grayish, usually larger and situated much deeper in the cutis.

Bowen's Disease. Presented by DR. SAMUEL FELDMAN.

B. K., a Polish housewife aged 57, states that she first noticed a lesion about two years ago. It began as a small patch and has gradually increased to its present size. There has never been any itching, burning or pain at the site of the lesion. On the outer surface of the right thigh there is a single round patch about 3 by 3½ inches (7.5 by 9 cm.) with a sharply defined border. The color is light red, but there is a brownish tinge near the margin. The surface is not smooth. There are a number of flat elevations, some of which are prominent, protruding 4 or 5 mm. above the surface; one of these flat tumors, located in the center of the patch, is ulcerated. In addition to the irregularities, the surface of the patch is covered by scales and yellowish adherent crusts.

The histologic examination showed edema of the rete, but the intercellular bridges were distinct. The rete pegs were enlarged. In some areas the cells of the rete were not uniformly stained. A number of cells were seen to be vacuolated, and a hyperchromatic nucleus was located eccentrically within the vacuole. Mitotic figures were occasionally encountered. There were edema and dilatation of the blood vessels in the cutis, and cellular infiltration was present. This was located not about the blood vessels but directly beneath the epithelium. The infiltrate consisted of lymphocytes, fibroblasts and a large number of plasma cells.

DISCUSSION

DR. ADOLPH ROSTENBERG: From the clinical appearance alone I should agree with the diagnosis of Bowen's disease. Of course, histologic examination is necessary in proving the diagnosis.

DR. WILBERT SACHS: I must confess that at times I cannot differentiate clinically between superficial basal cell epithelioma and Bowen's disease. If the specimen which I examined is from this patient, the diagnosis of Bowen's disease cannot be sustained. There is a marked inflammatory process underneath the

epidermis, and there is nothing in it to suggest Bowen's disease. I believe the condition may be basal cell epithelioma.

DR. SAMUEL FELDMAN: The diagnosis was thought to be either superficial basal cell epithelioma or Bowen's disease. Clinically, I believe one is justified in making a diagnosis of Bowen's disease, for crusts are usually not present in epithelioma. The histologic section, although poorly embedded, strongly suggested Bowen's disease.

Lichenoid Dermatitis (Vitamin Deficiency?). Presented by DR. PAUL GROSS.

B. B., a Negress aged 21, born in the United States, was first seen at the clinic of the Hospital for Joint Diseases on Aug. 2, 1937, with a generalized itchy cutaneous eruption of about two weeks' duration. The patient suffered during 1935 and 1936 from ulcerative colitis but has recovered under treatment. The diet has been fairly well balanced; she has meat only twice a week. On the body there is still an extensive eruption of well defined patches, consisting of numerous follicular papules the size of a pinhead. They have a scaly and at times spinulous top and by confluence produce a more diffuse scaling. An erythematous and scaly eruption is present in the nasolabial folds, on the chin and on the upper part of the neck. Except for markedly enlarged, cryptic tonsils and considerable obesity, the physical examination showed no abnormality.

Tuberculin tests with dilutions of 1:10,000 and higher gave negative reactions. Scrapings showed no fungi. The Wassermann and the Kahn reaction were negative. Examination of the eyes revealed only slight conjunctivitis.

The histologic examination showed evidence of compact follicular plugging and parakeratosis, associated with fairly marked perifollicular and perivascular inflammation.

Since Sept. 30, 1937, the patient has been receiving injections of liver extract and cod liver oil by mouth.

DISCUSSION

DR. WILBERT SACHS: I suggest the diagnosis of lichen spinulosus, which the pathologic examination corroborated.

DR. SAMUEL FELDMAN: The clinical picture is that of lichen spinulosus. This disease was described originally as a disease of childhood. It occurs in repeated acute attacks of well circumscribed patches, made up of numerous discrete acuminate spinous papules. Recently the scope of the title has been widened to include a similar condition in adults, but it must be borne in mind that a difference between the disease in children and that in adults, at least in etiology, may exist. The eruption in this patient may well fit the condition described as lichenoid dermatitis due to vitamin deficiency. In a case under my observation there was a resemblance to Darier's disease, and after the administration of extract of the whole adrenal gland the eruption cleared. Endocrine disturbances as well as vitamin deficiencies may cause similar conditions.

DR. LOUIS CHARGIN: I agree with the diagnosis of avitaminosis.

DR. PAUL GROSS: This patient presents clinically and histologically a follicular keratosis which can well be called lichen spinulosus, especially since the diagnosis of lichen scrofulosus can be excluded histologically. The eruption does not conform to the description of a deficiency of vitamin A in the skin; therefore, I am trying to study and treat this condition as a manifestation of deficiency in both vitamins A and B. The history of ulcerative colitis in 1935 and 1936 and the patient's standard of living are points in favor of my hypothesis.

Pityriasis Rubra Pilaris Treated with Liver Extract. Presented by DR. HENRY SILVER.

H. N., a housewife aged 40, a native of Hungary but a resident of the United States for the past twenty-three years, was admitted to the clinic of the Mount

Sinai Hospital on May 27, 1937. A hysterectomy was performed seventeen years ago. For many years the patient has been suffering from hypertrophic arthritis of the wrists, the knees and the toes.

The cutaneous eruption has persisted for the past thirteen years without remission. It is fairly generalized, though more pronounced on the face, the chest, the arms and the legs. The more severely involved areas are uniformly red and scaly. At the borders of the lesions there are hyperkeratotic follicles on an erythematous base. The nails are pitted, striated and dry. Characteristic keratotic follicles are present on the backs of the proximal phalanges of the fingers. The palms and the soles are thickened and scaly. The patient has frequented the clinics of many hospitals of this city.

The basal metabolic rate was + 19 per cent on July 14, 1937, and + 3 per cent on July 28, 1937. The blood pressure was 100 systolic and 70 diastolic. Examination of the blood and of the urine showed no abnormality.

Treatment with biweekly subcutaneous injections of 0.2 cc. of liver extract was instituted. To date the patient has received eighteen injections. The eruption has faded considerably, especially on the extremities and to a lesser degree on the scalp, the face and the trunk.

DISCUSSION

DR. PAUL GROSS: I have no intention of considering typical pityriasis rubra pilaris of thirteen years' duration as a disease due to vitamin deficiency and therefore am skeptical as to the benefits to be obtained with liver extract. The case which I presented last year and other instances of follicular keratosis resembling pityriasis rubra pilaris but lacking some of its important characteristics should be studied from the angle of vitamin deficiency and response to administration of liver extract.

DR. HENRY SILVER: I was much impressed with the good results obtained from administration of liver extract by Drs. Gross and Curth in the case presented before this society April 23, 1936 (ARCH. DERMAT. & SYPH. **35**:542 [March] 1937), that of a generalized follicular eruption diagnosed as pityriasis rubra pilaris (Devergie), accompanied with psoriasis. After injections of liver extract the follicular erythematous eruption disappeared, but the psoriasis remained. There is no question as to the diagnosis of pityriasis rubra pilaris (Devergie) in this case. There seems to be some improvement in certain areas, particularly on the extremities.

Pityriasis Lichenoides et Varioliformis Acuta. Presented by DR. ADOLPH ROSTENBERG.

This patient, a boy aged 8 years, presents an eruption which appeared in April 1937. The eruption is diffuse and consists of macular and papular lesions which vary in type. Some show pityriasiform scaling; others are crusted and seems to be the remnants of vesicles. At present there are on the left elbow lesions which show a necrotic center.

DISCUSSION

DR. PAUL GROSS: I suggest that this condition be called parapsoriasis with occasional varioliform lesions. I described a case like this one (ARCH. DERMAT. & SYPH. **23**:33 [Jan.] 1931) and separated the condition from the acute variety.

Generalized Tinea Corporis in Six Members of One Family. Presented by DR. CHARLES WOLF.

The father, aged 39, and three children, aged 2½, 4 and 8 years, present generalized eruptions consisting of typical circinate lesions which involve mostly the trunk and the extremities. In the child aged 4 years the scalp shows numerous lesions. The eruption spread rapidly from an infected cat and then from one child to another, all within one week. Two other children with the disease remained at home.

Urticaria Pigmentosa (Acquired Type). Presented by Dr. Samuel Feldman.

M. H., a housewife, aged 25, born in the United States, presents an eruption which began about six years ago and was characterized by itching and the appearance of wheals. After the eruption subsided, a discoloration remained, which covered practically the entire body, reaching downward to below the knees. The face, the chest, the back and the upper and lower extremities are covered with small round or oval flat brownish-red macules.

The examination of the urine showed no abnormality. The blood count showed 85 per cent hemoglobin, 4,200,000 red cells and 8,000 white cells. The differential count showed 60 per cent polymorphonuclear leukocytes, 30 per cent lymphocytes and 10 per cent eosinophils. The chemical examination of the blood showed 70 mg. of sugar, 25 mg. of nonprotein nitrogen and 9 mg. of calcium per hundred cubic centimeters.

The microscopic examination showed slight edema of the cutis, vascular dilatation and a mild perivascular infiltration consisting mostly of lymphocytes. Mast cells were rarely encountered and only in the sections stained by the Unna-Pappenheim method.

Phenolphthalein Eruption (Following the Use of a Proprietary Laxative). Presented by Dr. Frank E. Cross.

A. M., a housewife aged 67, was in the habit of taking Humphrey's tablets no. 99, which contain phenolphthalein. About four months ago an erythematous eruption appeared and healed slowly. About two weeks ago the patient was given tablets containing 2 grains (0.13 Gm.) of phenolphthalein, and within twenty-four hours a severe bullous eruption appeared. It involves the backs of the hands and the extensor surfaces of the forearms. The lesions are sharply defined, violaceous and circinate and are surmounted by bullae which nearly cover the individual lesions. On the back of the hands the lesions coalesce to form large plaques.

Book Reviews

Some **Fundamental Aspects of the Cancer Problem** (Symposium Sponsored by the Section on Medical Sciences of the American Association for the Advancement of Science, Dec. 29, 1936, to Jan. 1, 1937). Edited by Henry Baldwin Ward. Price, paper, $2; cloth, $2.50. Pp. 248, with illustrations. New York: The Science Press, 1937.

Thirty-one papers on various phases of cancer which were presented before the Section on Medical Sciences at the December 1936 meeting of the American Association for the Advancement of Science have been collected and published in book form by the association. Each one represents the views of the particular writer as to his own branch of the subject.

The book is divided into parts dealing with heredity and constitutional factors, with the induction, stimulation and inhibition of tumorous growths, with the metabolism of cancerous tissue, with radiation and with the problem of cancer in general.

In the section on heredity Slye and Little discuss their opposing views regarding the dominant factors in the heredity of cancer. The reader, therefore, may elect to believe with Maud Slye that there are no extra chromosomal influences but specific transmissible recessive characters which may be suppressed by a dominant one, or with Little that the growth of cancer depends chiefly on influences transmissible through the maternal line by some agents outside the chromosomes.

Five papers discuss in clear and concise terms various other biologic phases of the subject.

Nine are devoted to explaining the various factors associated with the induction, stimulation and inhibition of tumors. Wood, in a general article on the chemical phases of carcinogenesis, summarizes historically the part chemistry plays in the etiology of cancer.

In a discussion of the relation of the endocrine glands to carcinoma Geschickter and Astwood properly state that the application of endocrinology to cancer is limited but that, nevertheless, the newer knowledge obtained by the study of endocrine effects on the tissues is distinctly valuable at times in distinguishing benign from malignant conditions. Other authors, however, seem to discern a reasonable basis for acceptance of a hormonal background for carcinoma in many instances.

In the section on radiation are covered purely physical and biologic aspects of radiation, the question of applying heat and radiation therapeutically and a report on the progress made in the study of poisoning with radium.

Taylor discusses means of determining the quality of roentgen radiation by filtration. Its importance to the radiologist, Taylor states, lies in the fact that x-ray quality means "some descriptive index which will permit reproduction of one of the essential treatment factors, namely, the 'penetration' or 'depth dose.'" This Taylor proceeds to obtain in accordance with his suggested method.

Numerous methods have been advanced for augmenting the value of irradiation in the treatment of malignant conditions. Jacobs and Warren offer a method of combining fever therapy with roentgen irradiation which they have found highly efficacious in animals. Whether such results can be obtained in man is still a question.

The social effect of cancer is discussed by Dublin in a statistical analysis of mortality due to cancer. He concludes that, although the actual death rate from the disease probably is not increasing, the number of fatalities will unquestionably continue to mount from year to year as the proportion of older people in the population grows larger. Dublin states, correctly, that the national movement

for better control of cancer should be stimulated by the knowledge of the fact that real gains against the disease have been achieved with the scientific methods at hand.

Schiller offers some newer conceptions as to the cause of cancer to replace what he terms the overestimated importance of irritation as an etiologic factor.

On the whole, this compilation of the various essays presented at the symposium is well worth careful reading by all who are interested in the study of cancer from every angle.

As the editor remarks, these papers furnish abundant evidence that the field of research on cancer is so broad and diversified that in the present state of knowledge differences of opinion concerning the merit of individual conclusions cannot but occur.

Twenty-Five Years of Health Progress. A Study of the Mortality Experience Among the Industrial Policyholders of the Metropolitan Life Insurance Company, 1911 to 1935. By Louis I. Dublin and Alfred J. Lotka. Pp. 596. New York: Metropolitan Life Insurance Company, 1937.

In spite of dealing mainly with statistics, this volume is surprisingly readable and is a valuable book of reference. It is a review of the mortality among holders of the industrial policies of a large insurance company during the twenty-five years from 1911 to 1935. The authors state that no other data concerning the mortality of such a large group of insured persons over such a length of time exist. In 1935 there were 17,000,000 policy holders. The book is written for health officers, physicians, sociologists, life insurance officials and others interested in the health of wage earners.

An interesting chapter is devoted to the progress in health during a quarter of a century, and another chapter discusses the trend of longevity during this period. In a discussion of various diseases or accidents which cause death, statistics are given concerning age, sex, color and the trend of mortality.

Brief chapters on cancer of the skin and on syphilis are of special interest to dermatologists and syphilologists. In the twenty-five years 4,315 deaths occurred from cancer of the skin—1.6 per cent of deaths from all forms of cancer. Approximately 45 per cent of these deaths occurred in persons of 75 years or more. In the white race the average death rate for men was almost twice that for women. The statistics showed that Negroes, as is well known, are "relatively immune" to cancer of the skin. The trend of mortality from this disease during the past twenty-five years was "significantly downward" among white policyholders. It was thought that this was probably due both to a decreased incidence of the disease and to improvement in treatment. It was suggested that elimination of occupational hazards may have been contributory. The two important factors in the decrease in cutaneous cancer were considered to be educational propaganda and improvement in therapeutic methods.

Syphilis, including tabes dorsalis and dementia paralytica, caused 44,480 deaths during the twenty-five years. "Because of the tendency of physicians to omit syphilis from the death certificate, the actual number of deaths from this cause is greatly in excess of the number recorded." Furthermore, the authors state that many deaths recorded as being due to hemorrhage, arteriosclerosis or cardiac disease were caused by syphilis.

The mortality from syphilis was highest in Negroes. In the twenty-five years it was four and one-half times as high in Negroes as in white men and six times as high in Negroes as in white women.

Except for the first year of life, the greatest mortality from syphilis occurred in middle and later adult life. Since the World War there has been a substantial decrease in mortality in the wage-earning population. This decrease, however, is confined to the white race.

Directory of Dermatologic Societies *

INTERNATIONAL

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102—2nd Ave., S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. J. McGovern, President, 4005 Dorchester St., Montreal.
F. L. Boulais, Secretary-Treasurer, 2061 St. Denis St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Joseph V. Klauder, Chairman, 1934 Spruce St., Philadelphia.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: San Francisco. Time: June 13-17, 1938.

American Academy of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: St. Louis. Time: November 1938.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: San Francisco. Time: June 1938.

American Dermatological Association

James Herbert Mitchell, President, 25 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: Del Monte, Calif. Time: June 8-11, 1938.

Society for Investigative Dermatology

George M. MacKee, President, 200 W. 59th St., New York.
S. M. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.

Mississippi Valley Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Charles R. Mitchell, President, 311 Broadway, Paterson.
Louis J. B. LeBel, Secretary, 165 Grant Ave., Nutley.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville, Fla.
Joseph A. Elliott, Secretary, Professional Bldg., Charlotte, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

Harry M. Robinson, Chairman, 106 E. Chase St., Baltimore, Md.
Winston U. Rutledge, Secretary, 332 W. Broadway, Louisville, Ky.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Stanley O. Chambers, Chairman, 727 W. 7th St., Los Angeles.
Nelson Paul Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.
Place: Pasadena. Time: May 9-12, 1938.

Connecticut State Medical Society, Section on Dermatology

E. Myles Standish, Chairman, 179 Allyn St., Hartford.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.
Place: New Haven. Time: May 19, 1938.

Florida Society of Dermatology and Syphilology

C. A. Andrews, Chairman, 706 Franklin St., Tampa.
Lauren Sompayrac, Secretary, 204 Laura St., Jacksonville.
Place: Jacksonville. Time: June 1938.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

George A. Dix, President, 6 Ashland St., Worcester.
J. Harper Blaisdell, Secretary, 45 Bay State Rd., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Leo Spiegel, Chairman, 241 W. 100th St., New York.
Mark Heiman, Secretary, 600 Medical Arts Bldg., Syracuse.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

L. G. Beinhauer, Chairman, 5026 Jenkins Arcade Bldg., Pittsburgh.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.
Place: Scranton. Time: October 1938.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

G. Warren Hyde, Chairman, 2501 W. Grand Blvd., Detroit.
Ruth Herrick, Secretary, 26 Sheldon Ave., Grand Rapids.

MINNESOTA DERMATOLOGICAL SOCIETY

L. A. Brunsting, President, 102–2d Ave., S. W., Rochester.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Harry Green, President, Medical Arts Bldg., Tulsa.
M. O. Nelson, Secretary, Medical Arts Bldg., Tulsa.

TEXAS DERMATOLOGICAL SOCIETY

Bedford Shelmire, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Galveston. Time: May 9-12, 1938.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Herman E. Kittredge, President, 1835 I St., N. W., Washington, D. C.
I. Louis Sandler, Secretary, 1835 I St., N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Theodore Rosenthal, President, 115 W. 86th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.
Time: June 1938.

BROOKLYN DERMATOLOGICAL SOCIETY

David L. Satenstein, President, 57 W. 57th St., New York.
M. Edward Goebel, Secretary, 842 Union St., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Clarence H. Peachey, President, 197 S. Goodman St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Rudolph Ruedemann Jr., President, 256 State St., Albany.
Harry D. Parkhurst, Secretary-Treasurer, 264 Genesee St., Utica, N. Y.

CHICAGO DERMATOLOGICAL SOCIETY

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.
Place: Chicago. Time: Third Wednesday in January 1938.

CINCINNATI DERMATOLOGICAL SOCIETY

Leon Goldman, President, Doctors Bldg., Cincinnati.
George E. Clarke, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

Claude B. Norris, President, 244 Lincoln Ave., Youngstown, Ohio.
Clyde L. Cummer, Secretary, 1010 Hanna Bldg., Cleveland.
Place: Cleveland. Time: May 26, 1938.

Detroit Dermatological Society

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: May 1938.

Los Angeles Dermatological Society

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Andrew J. Gilmour, Chairman, 121 E. 60th St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.
Place: New York. Time: May 1938.

Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 450 Sherbrooke St., E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Louis Chargin, Chairman, 1 W. 85th St., New York.
Harry C. Saunders, Secretary, 159 W. 87th St., New York.

New York Dermatological Society

Eugene F. Traub, President, 140 E. 54th St., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln.

Philadelphia Dermatological Society

Frank C. Knowles, Chairman, 2035 Spruce St., Philadelphia.
Thomas Butterworth, Secretary, 411 Walnut St., Reading, Pa.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

A. Fisher, President, 530½—5th Ave., McKeesport, Pa.
Francis P. Kenney, Secretary, Westinghouse Bldg., Pittsburgh.

St. Louis Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Norman Epstein, President, 450 Sutter St., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland.
Place: San Francisco. Time: Third Friday of November 1937.